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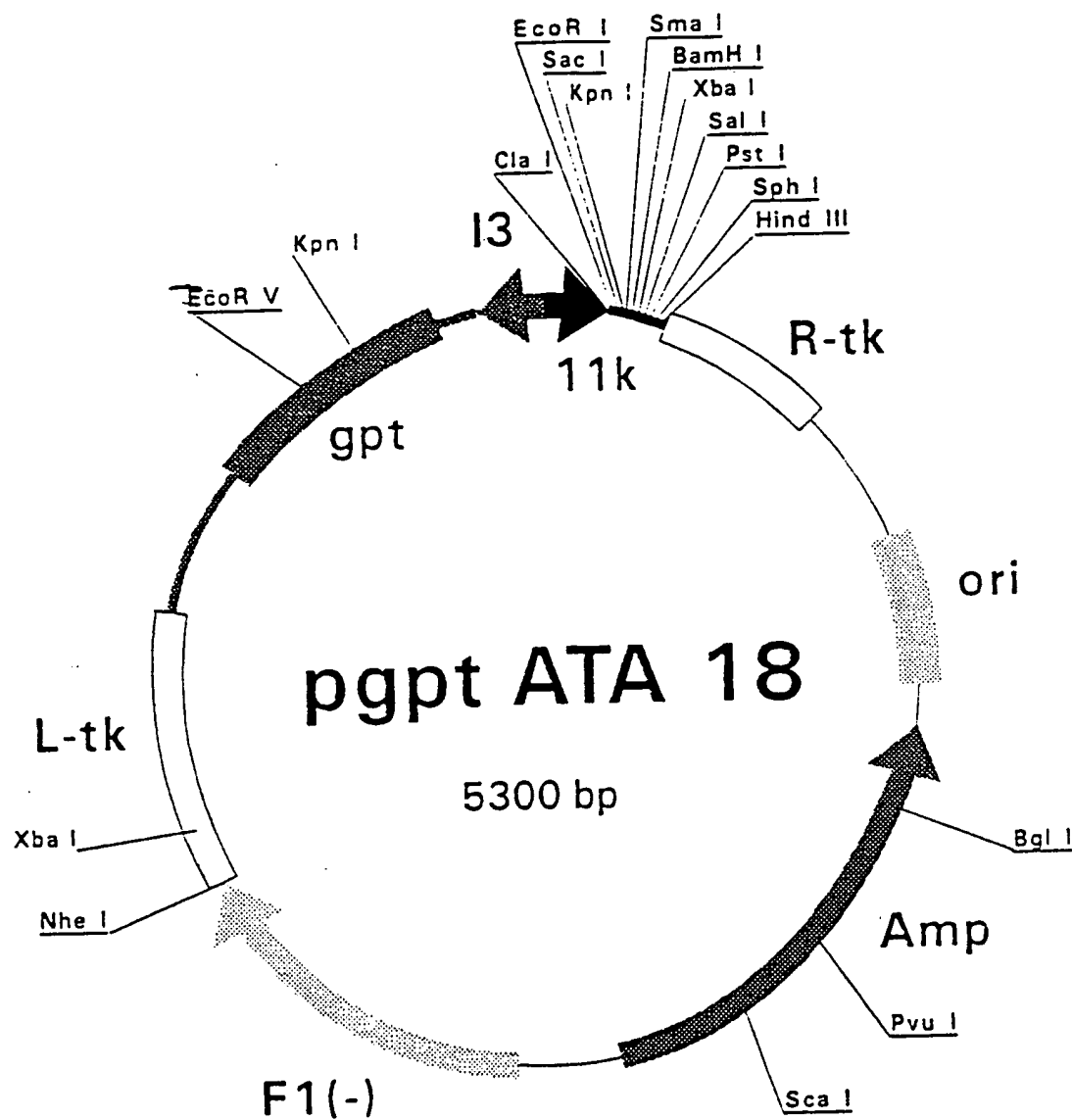


Fig. 1

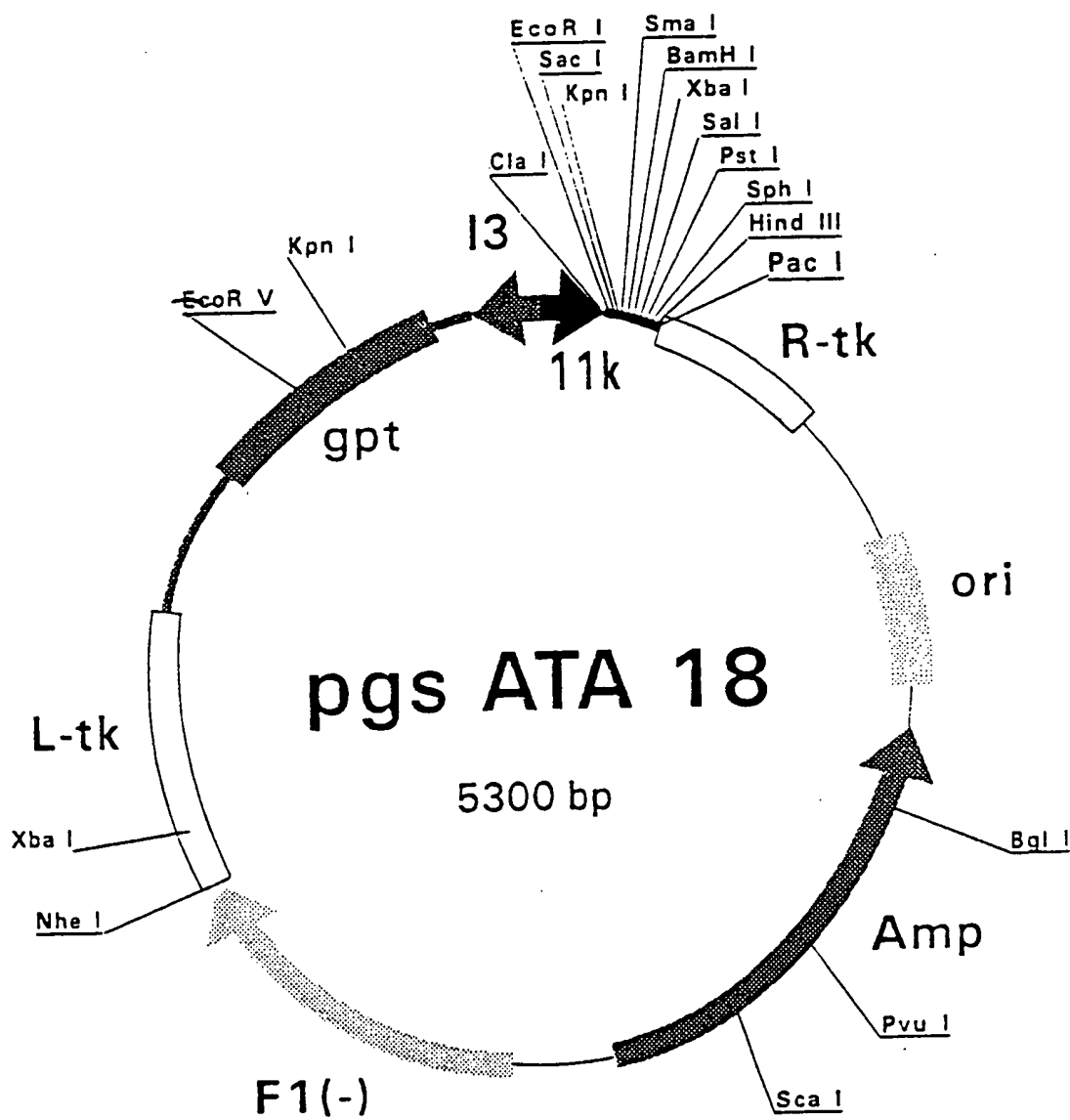


Fig. 2



SECRET

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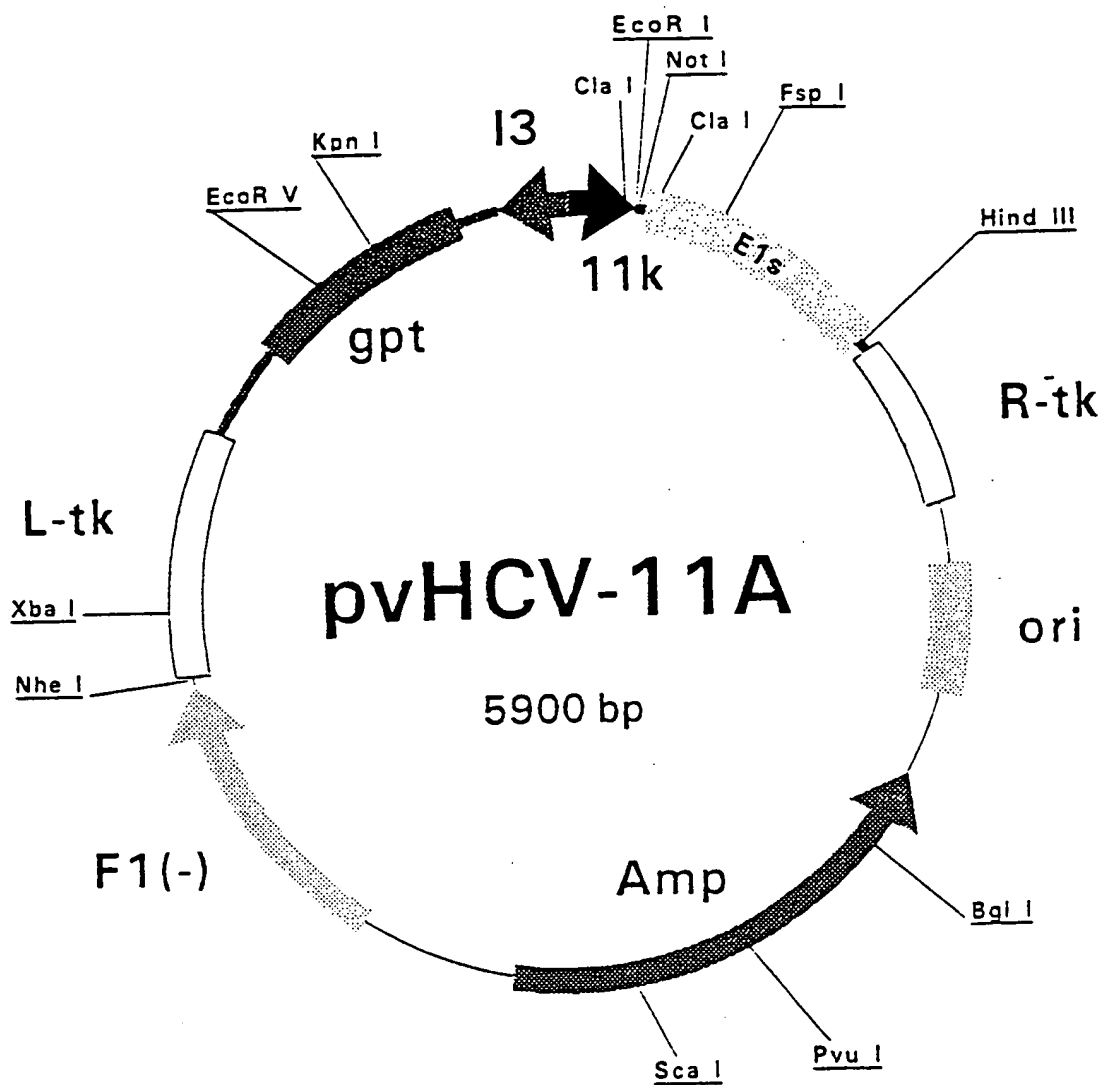
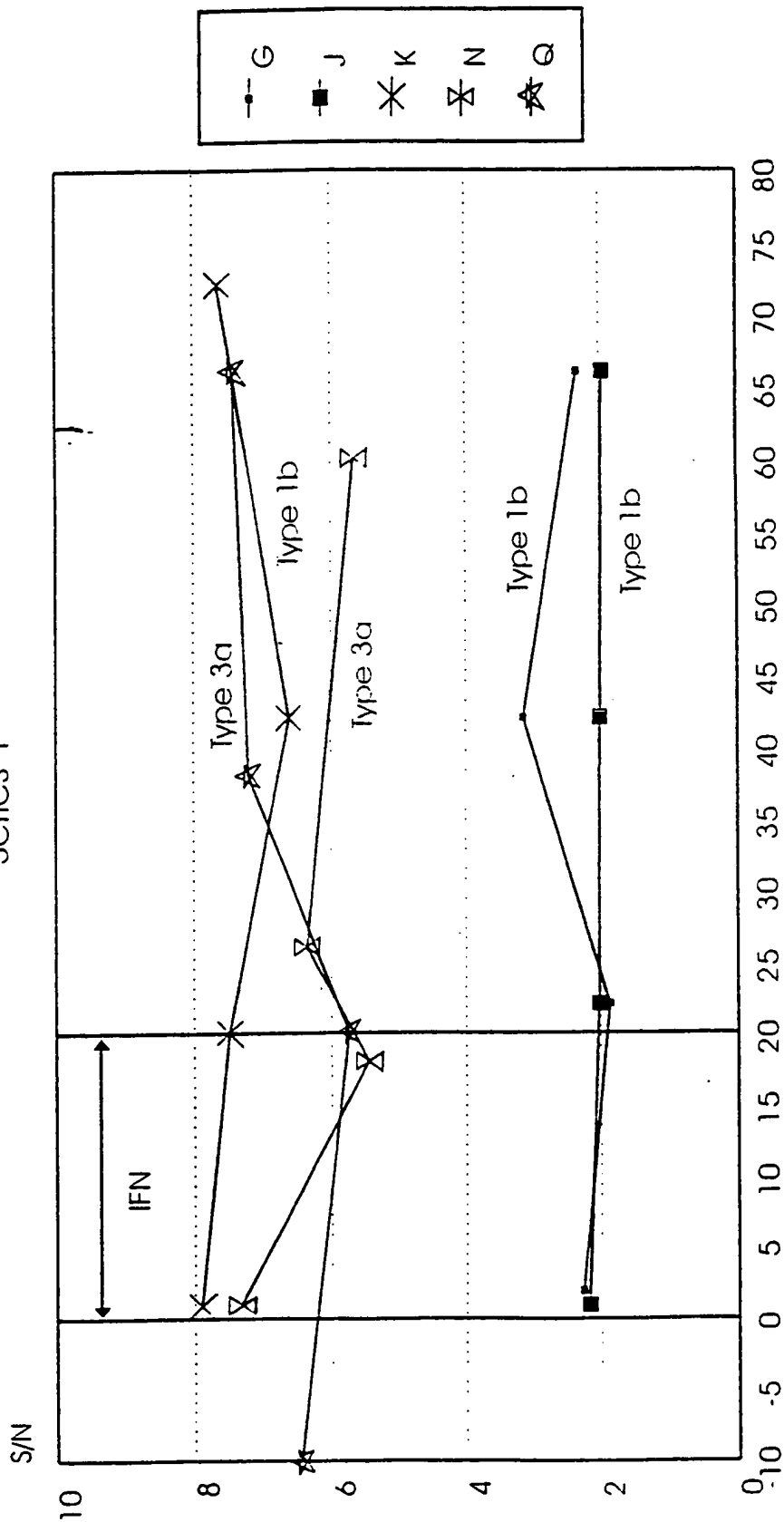


Fig. 4

Anti-E1 levels in NON-responders to IFN treatment

Series 1



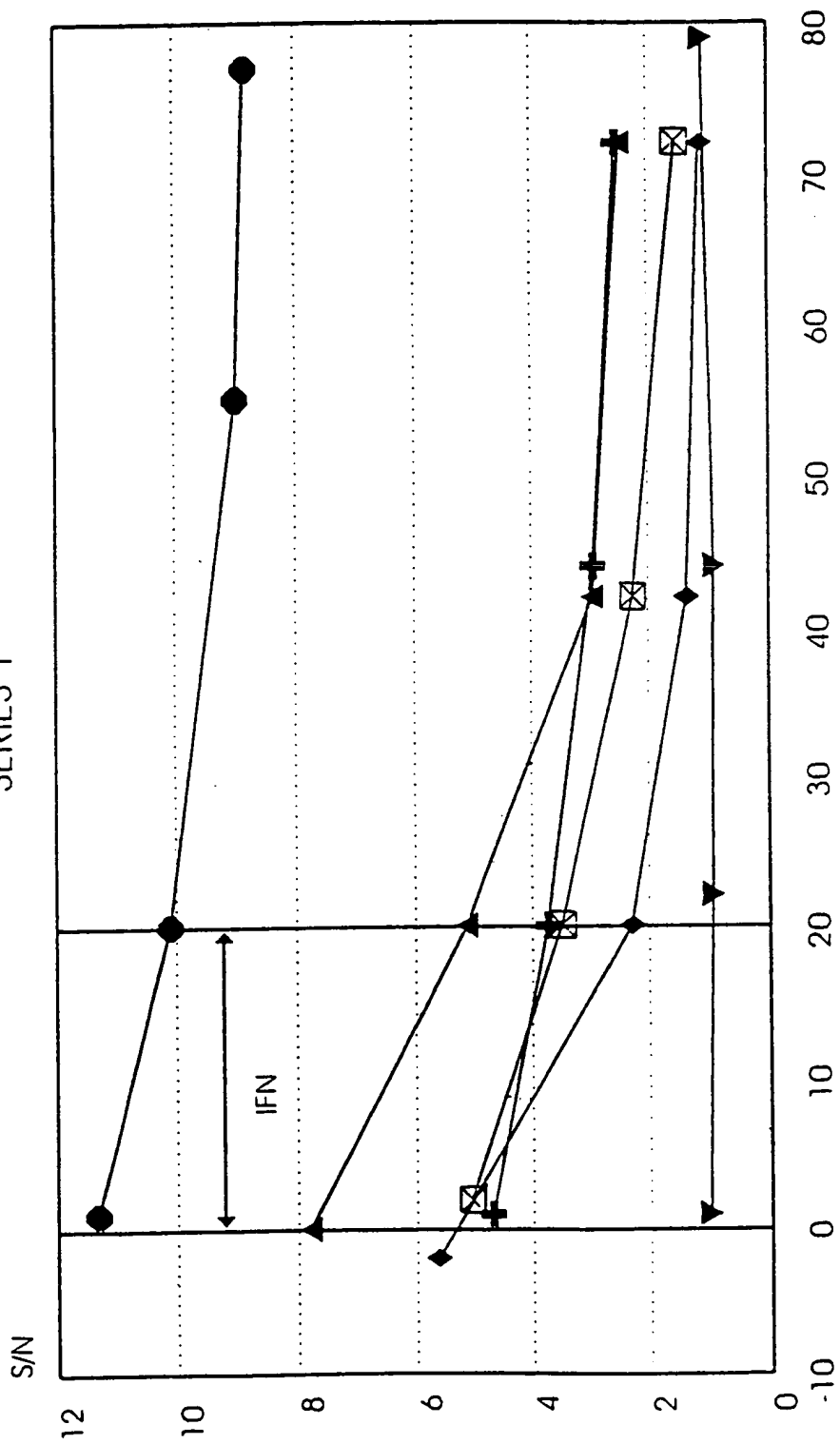
weeks after start of treatment

Fig. 5



Anti-E1 levels in RESPONDERS to IFN treatment

SERIES 1



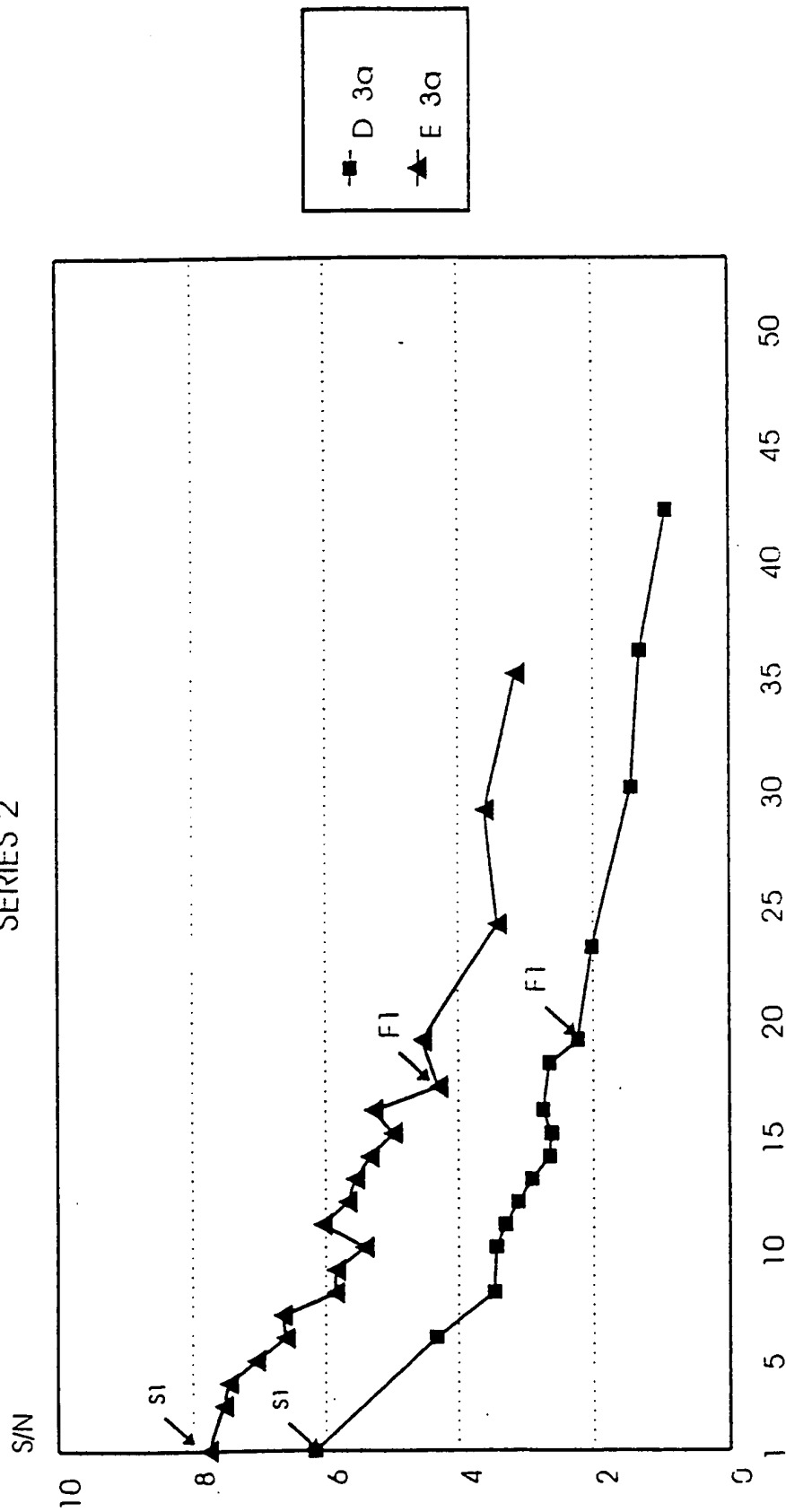
weeks after start of treatment

Fig. 6



Anti-E1 levels in patients with COMPLETE response to IFN

SERIES 2



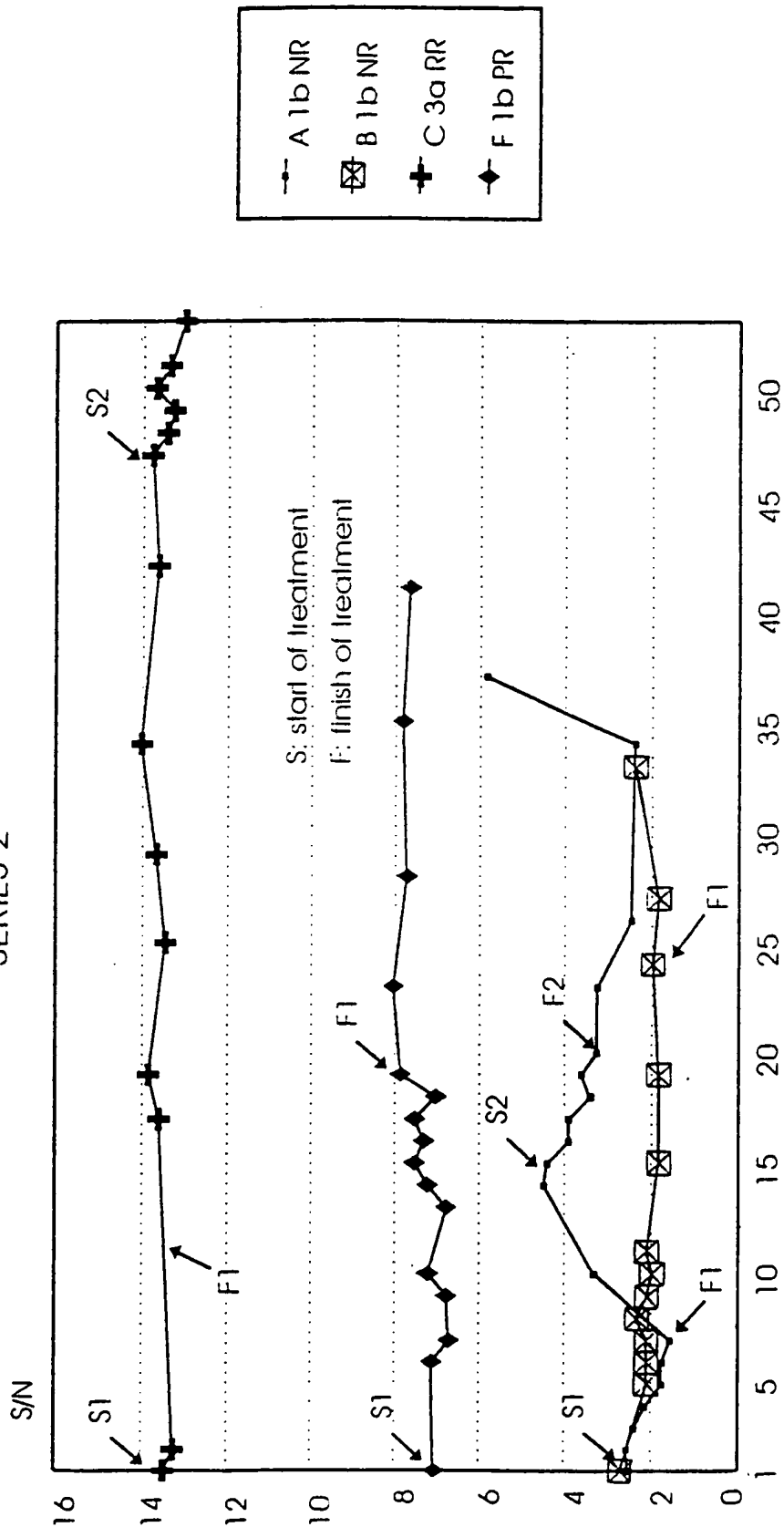
months after start of treatment

Fig. 7



Anti-E1 levels in INCOMPLETE responders to IFN treatment

SERIES 2



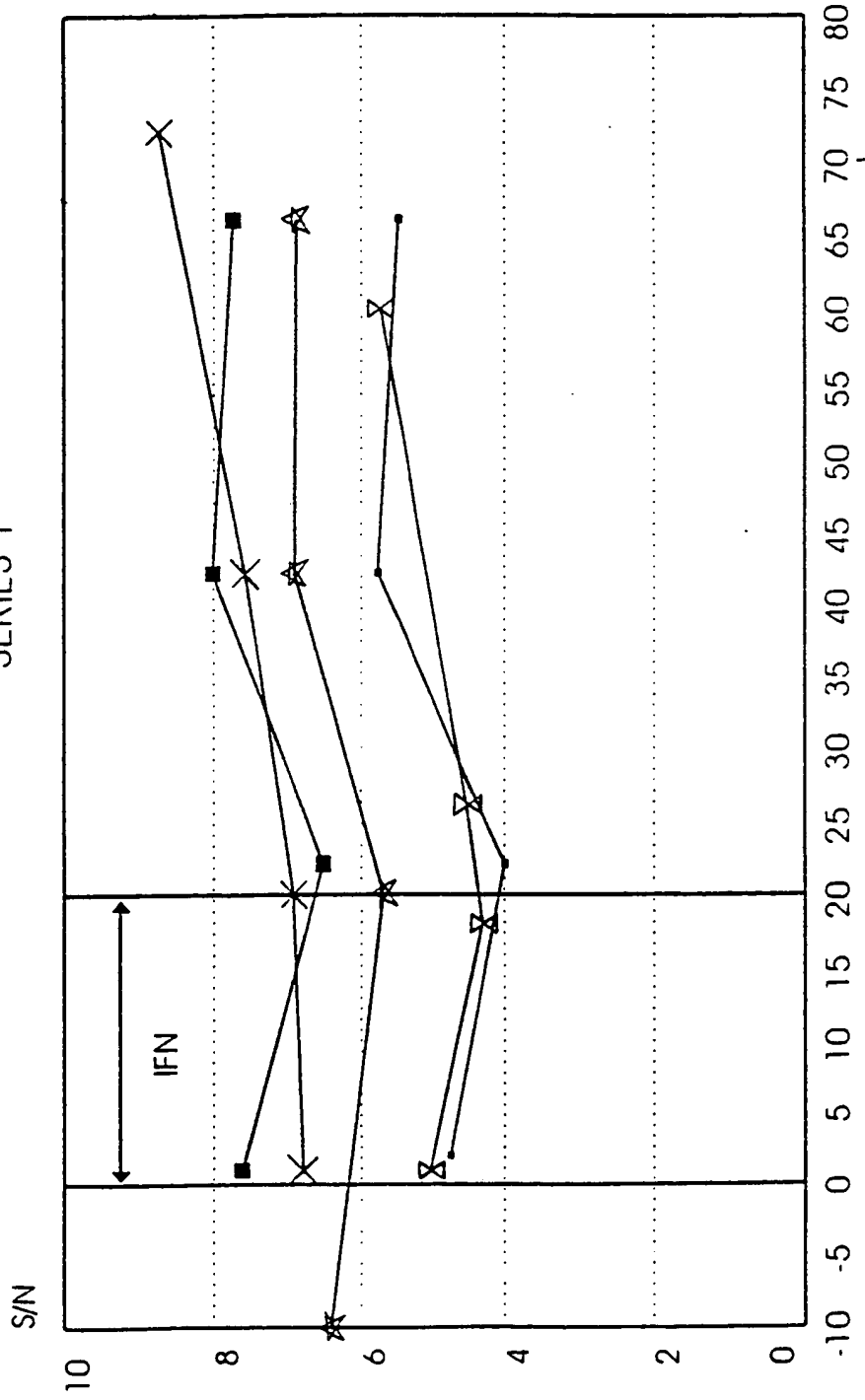
months after start of treatment

Fig. 8



Anti-E2 levels in NON-RESPONDERS to IFN treatment

SERIES 1



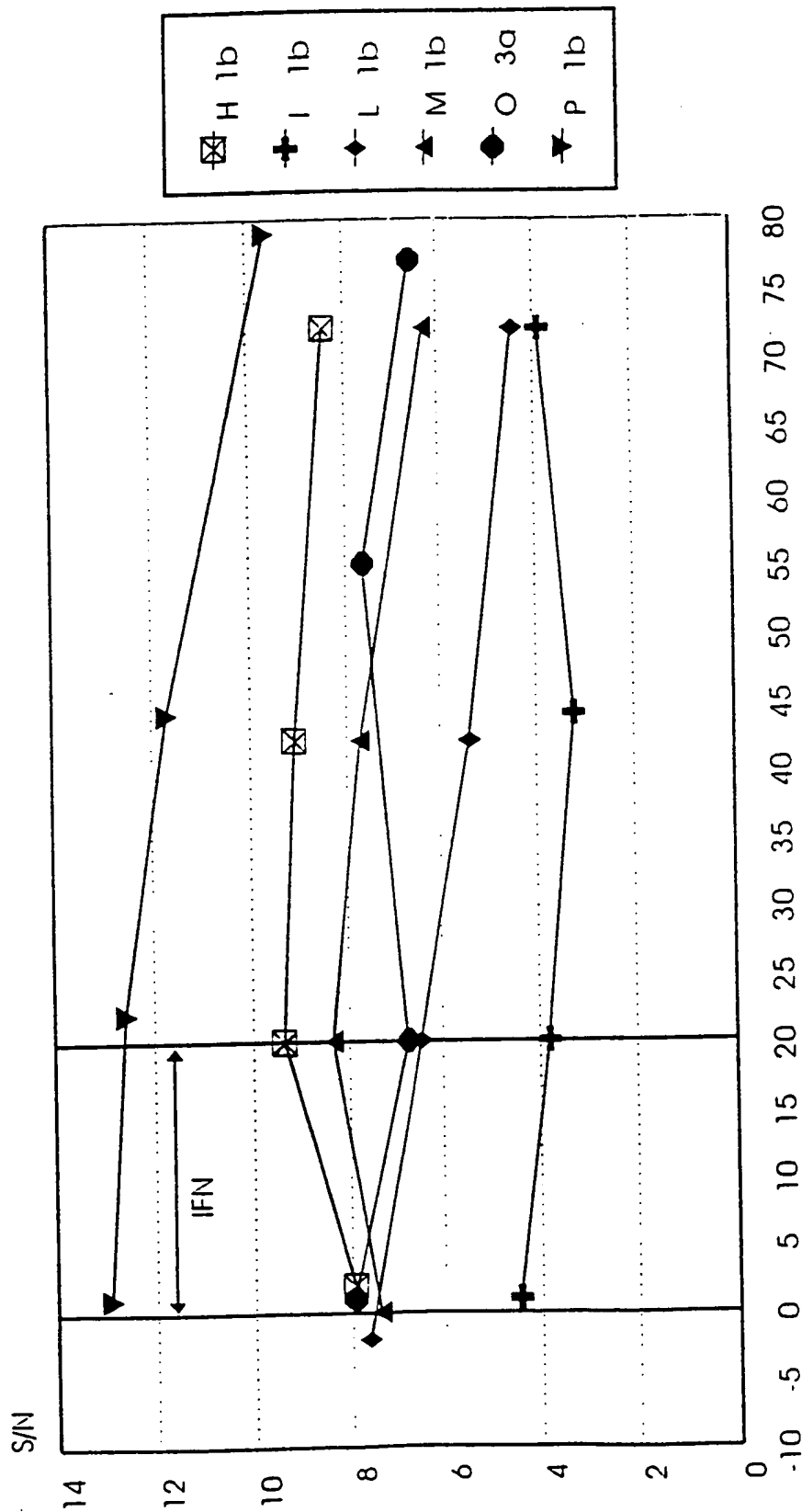
weeks after start of treatment

Fig. 9



Anti-E2 levels in RESPONDERS to IFN treatment

SERIES 1



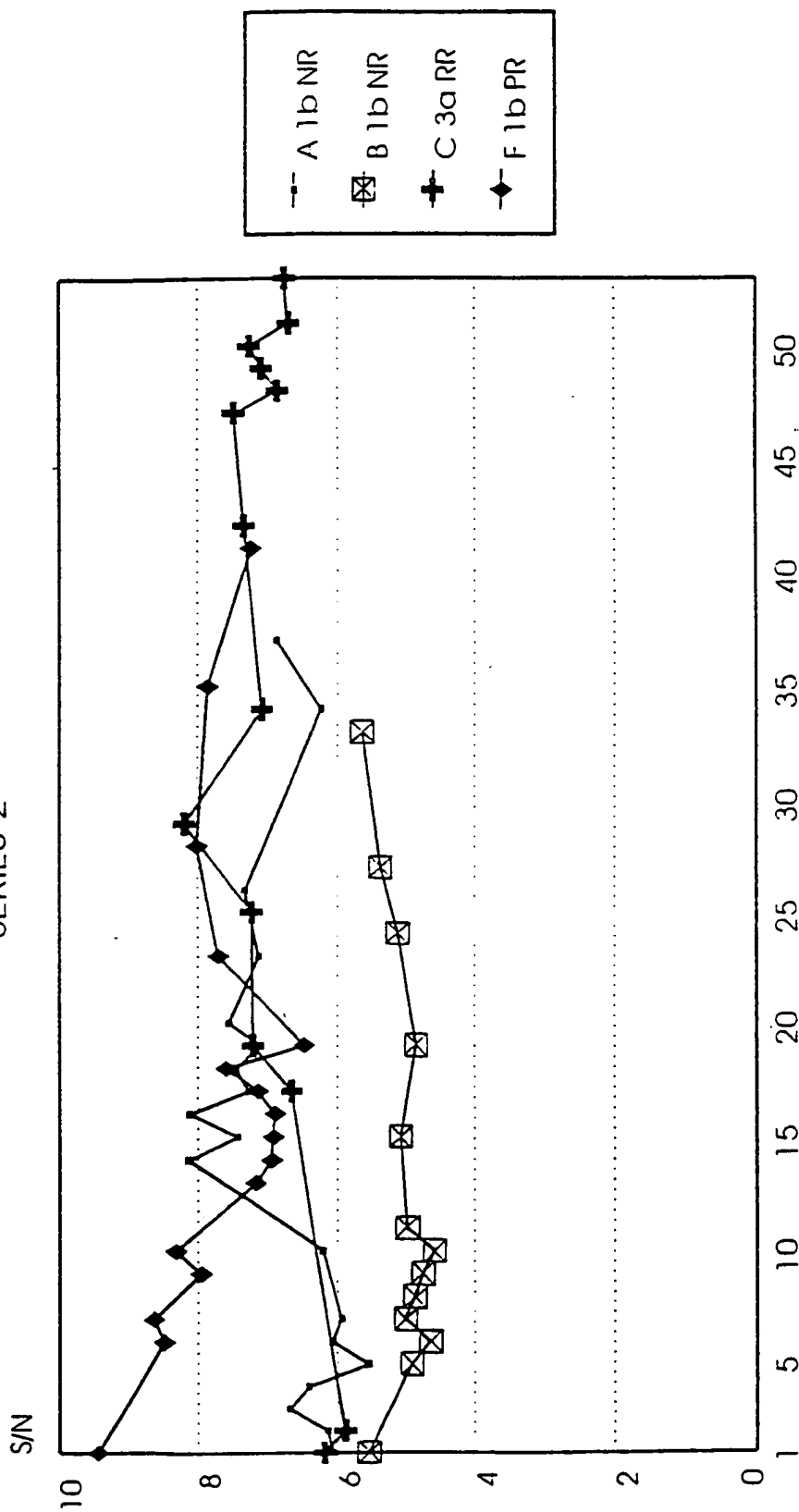
weeks after start of treatment

Fig.10



Anti-E2 levels in INCOMPLETE responders to IFN treatment

SERIES 2



months after start of treatment

Fig.11



Human anti-E1 reactivity competed with peptides

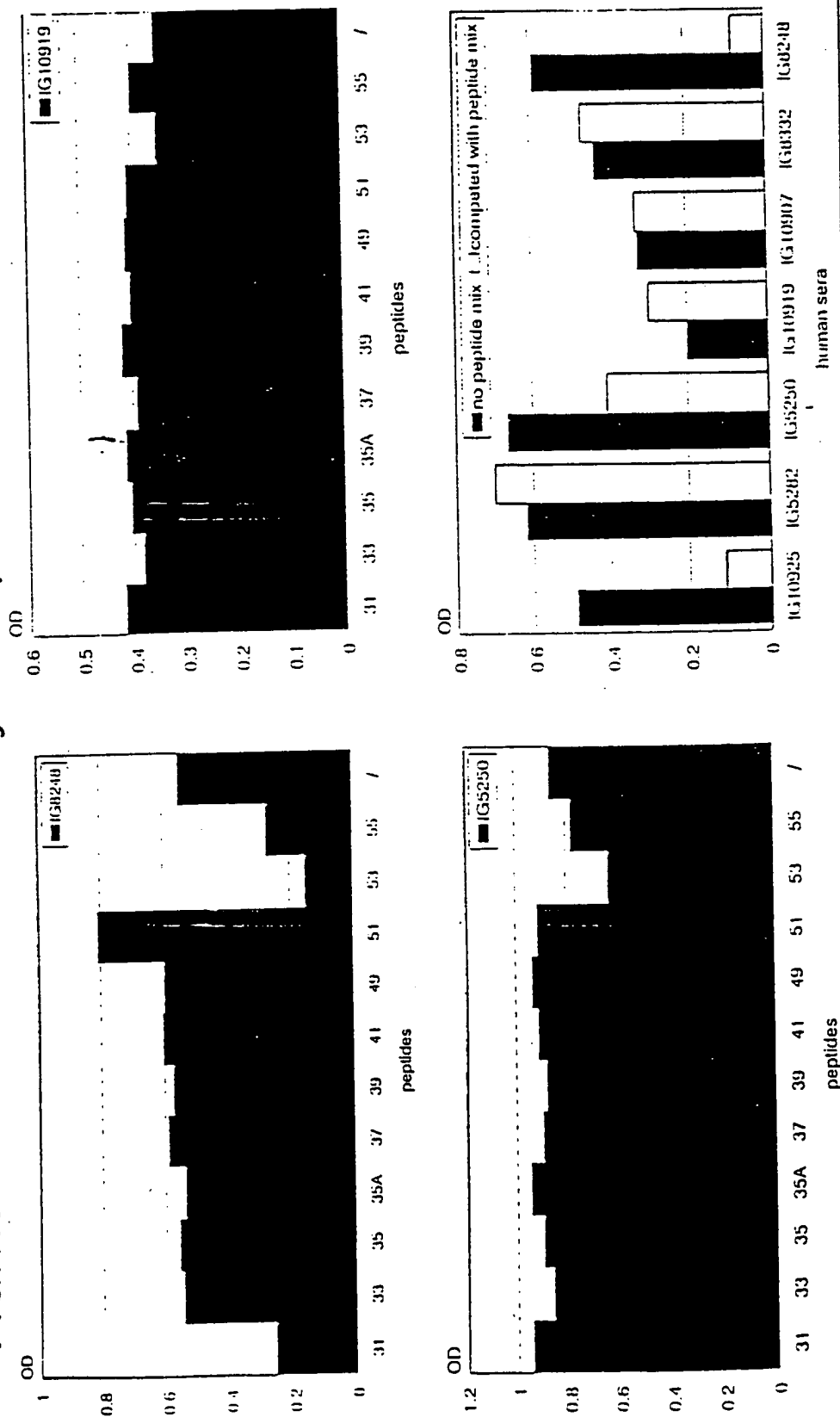


Fig.13

Competition of reactivity of anti-E1 Mabs with peptides

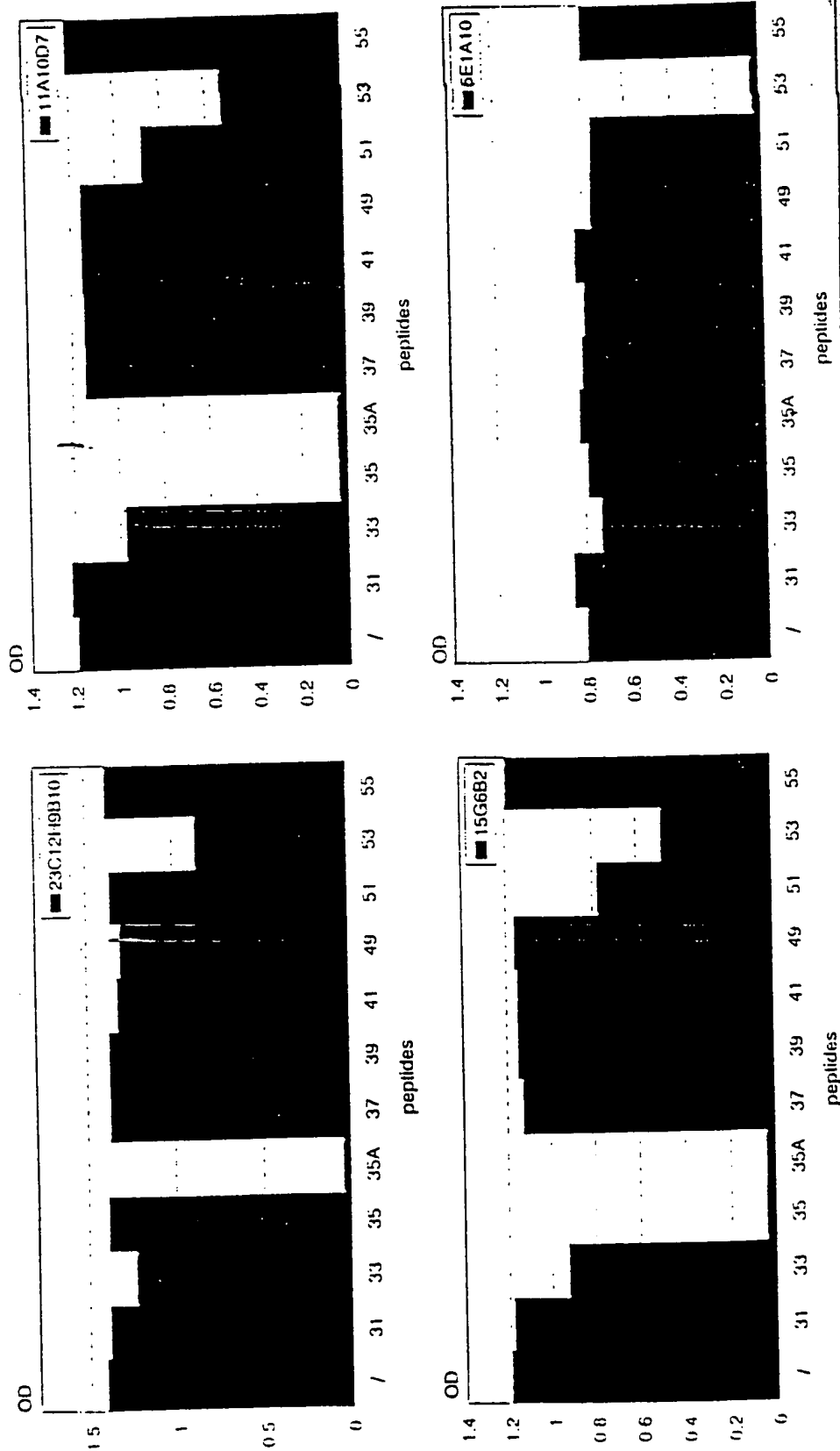
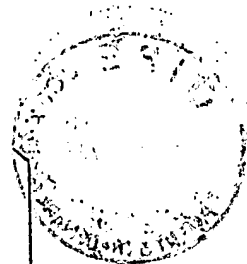
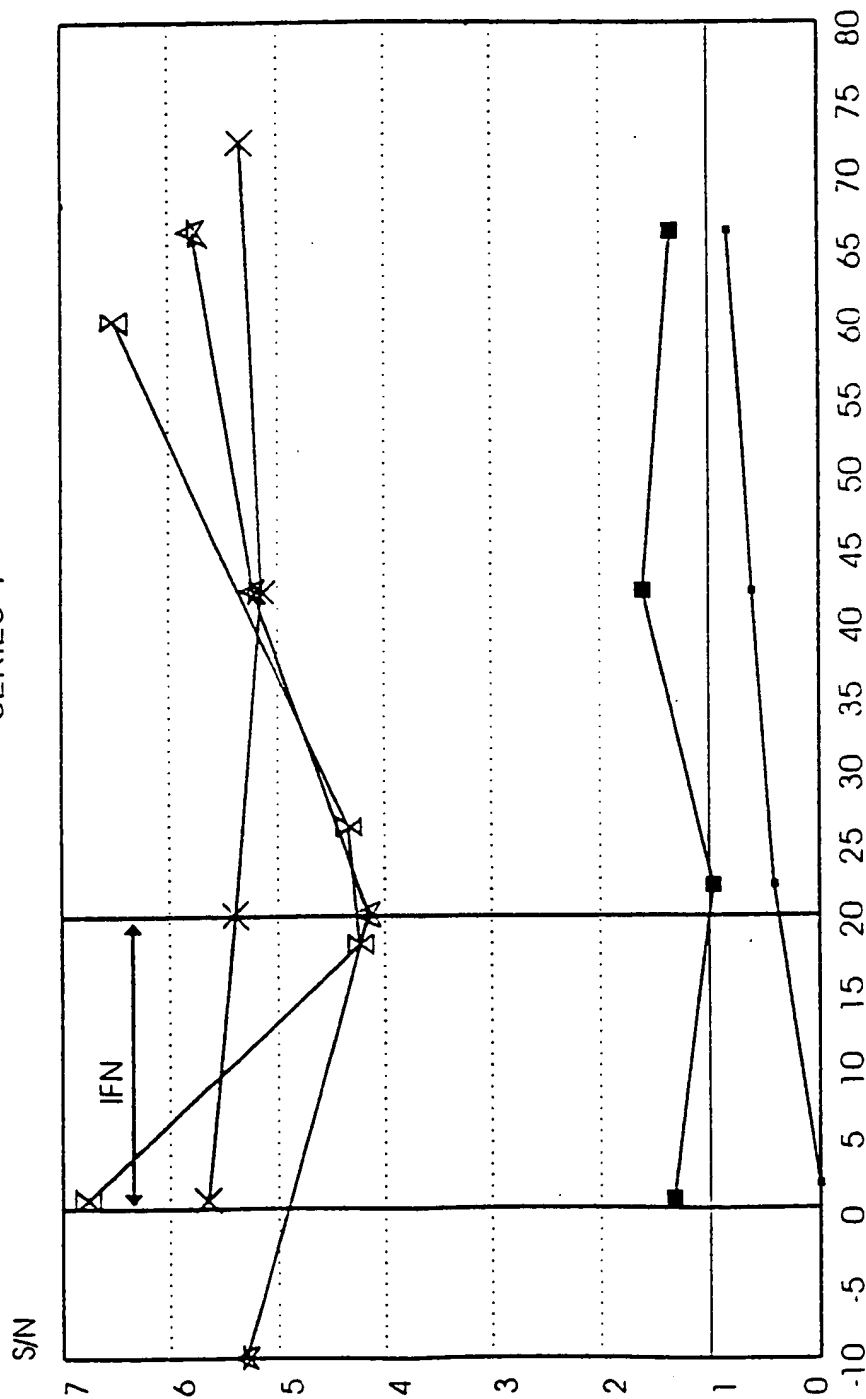


Fig.14



Anti-E1 (epitope 1) levels in NON-RESPONDERS to IFN treatment

SERIES 1



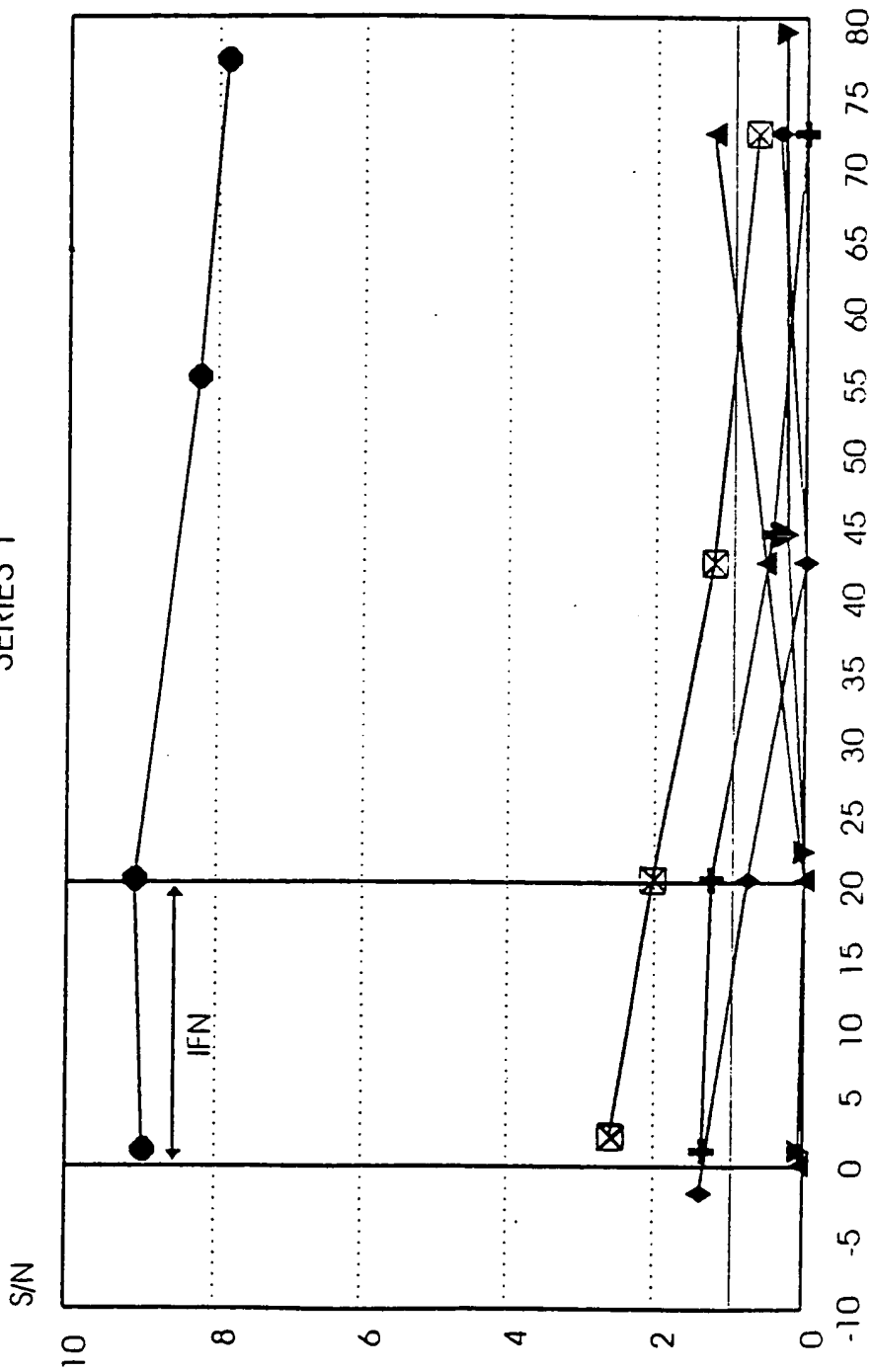
weeks after start of treatment

Fig.15



Anti-E1 (epitope 1) levels in RESPONDERS to IFN treatment

SERIES 1

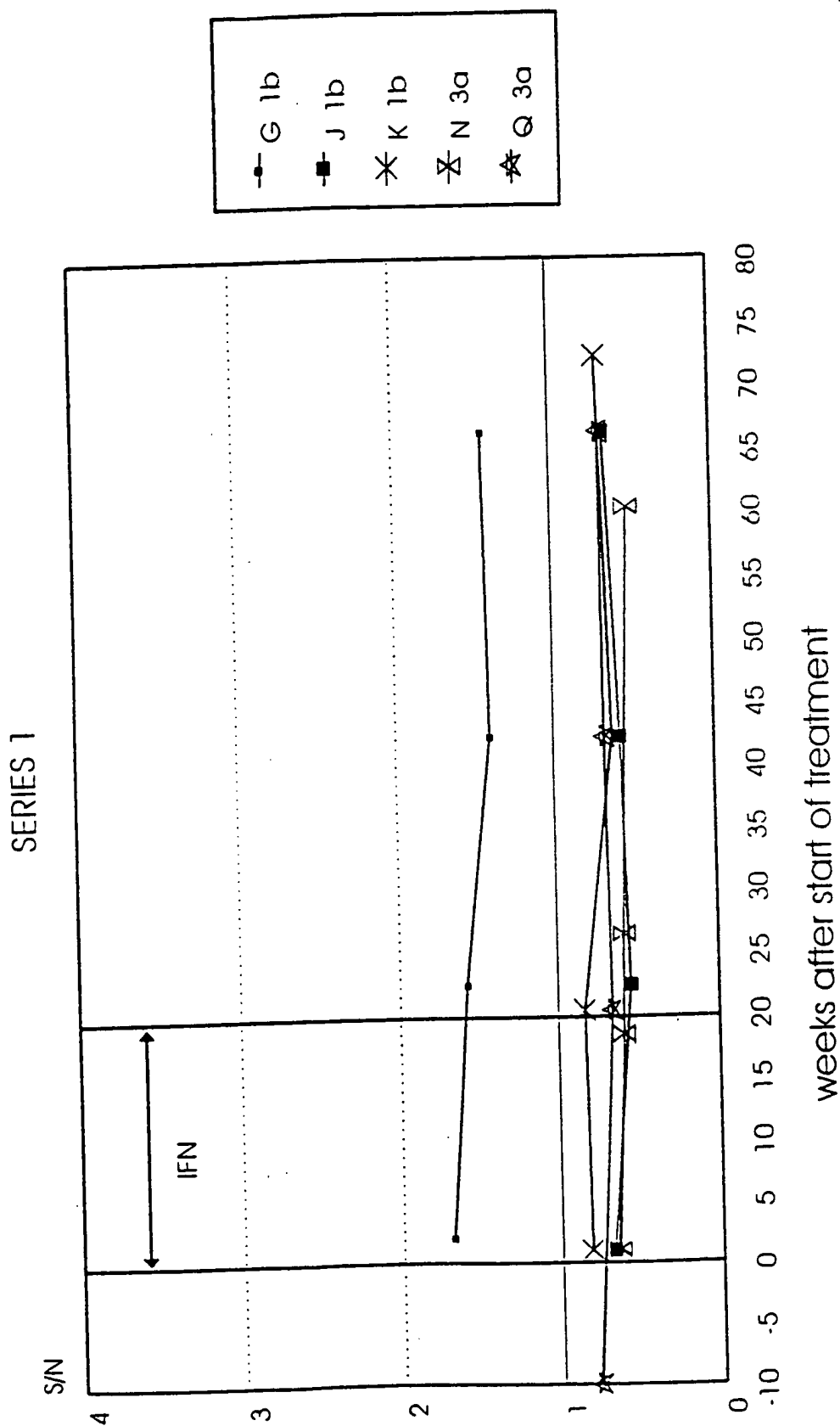


weeks after start of treatment

Fig.16

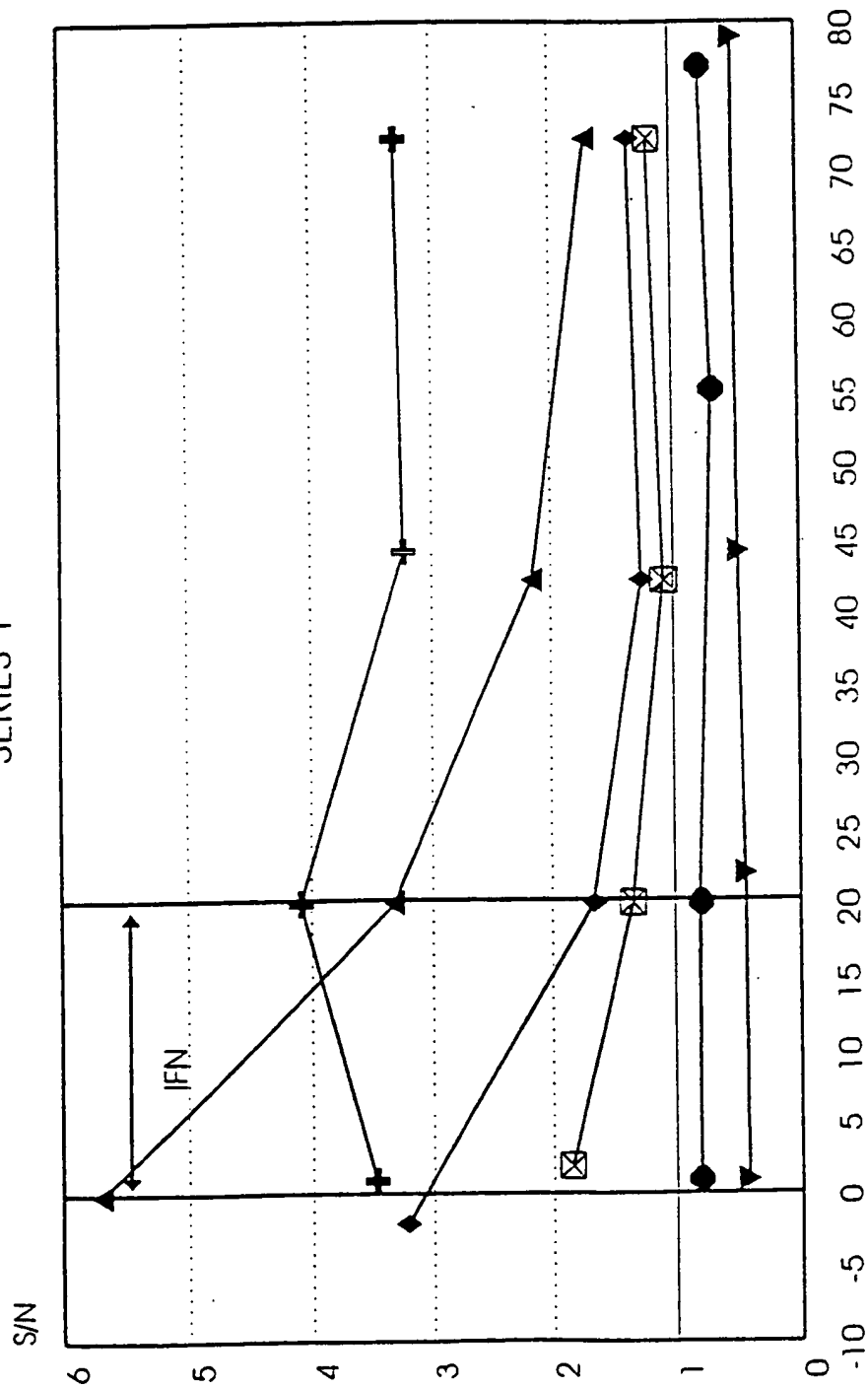


Anti-E1 (epitope 2) levels in NON-RESPONDERS to IFN treatment



Anti-E1 (epitope 2) levels in RESPONDERS to IFN treatment

SERIES 1



weeks after start of treatment

Fig.18

Competition of reactivity of anti-E2 Mabs with peptides

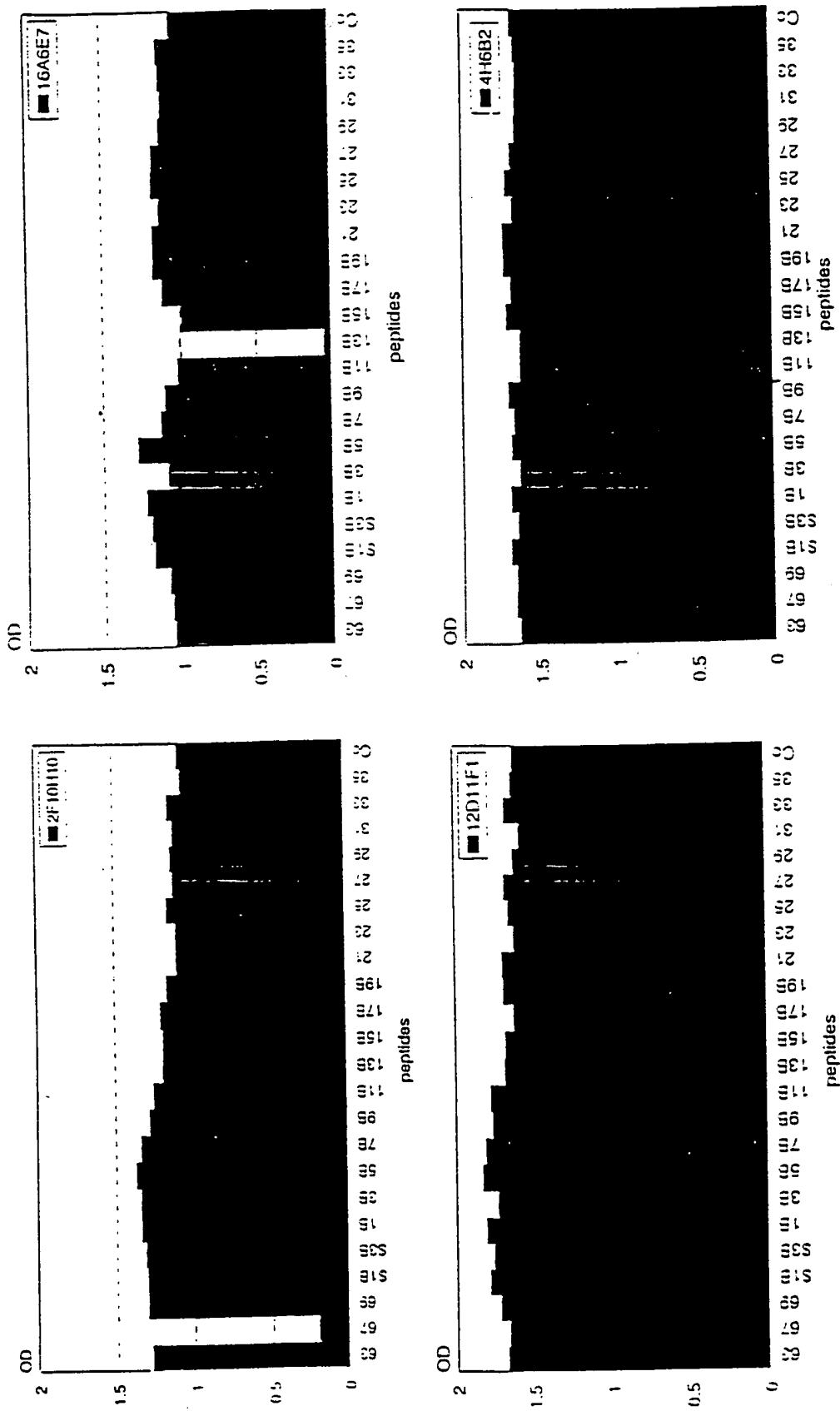


Fig.19



Human anti-E2 reactivity competed with peptides

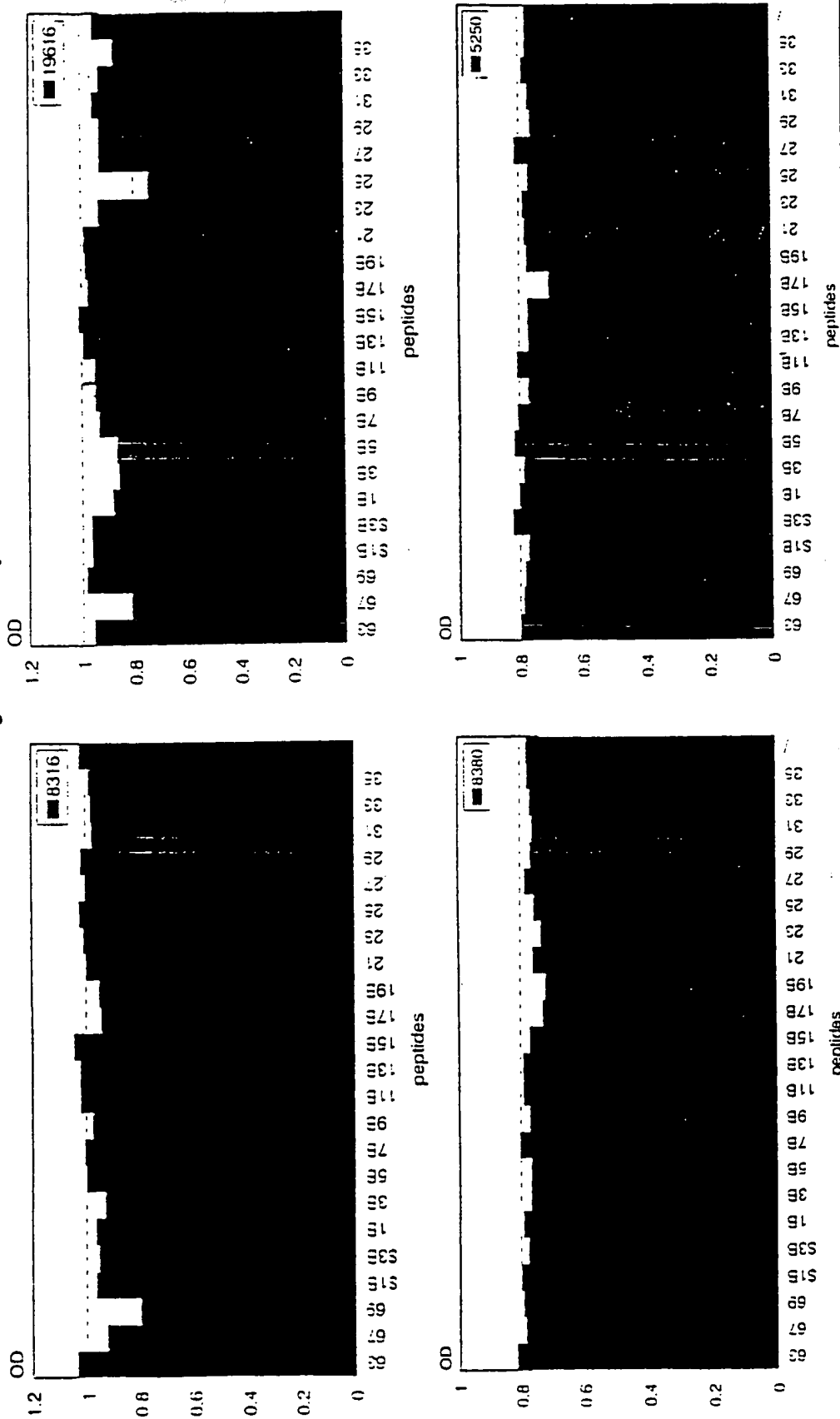


Fig. 20



Fig. 21A

Fig. 21B

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SEQ ID NO 7 (HCC111A)

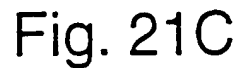
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SEQ ID NO 9 (HCCI12A)

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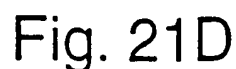
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SECRET



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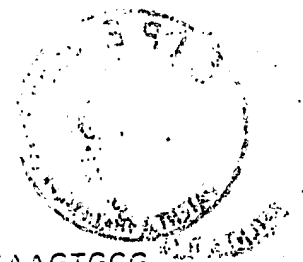
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GGTCTCGGAGGACGGCGTGAACATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCT

SECRET

Fig. 21E



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SEQ ID NO 27 (HCC140)

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SEQ ID NO 29 (HCC162)

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Fig. 21F

SEQ ID NO 31 (HCCI63)

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SEQ ID NO 33 (HCP109)

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SEQ ID NO 34 (HCP72)

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SEQ ID NO 35 (HCCL22A)

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SECRET

TCAAGGT

SECRET

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Fig. 21H



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SEQ ID NO 41 (HCC143)

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Fig. 21I



SEQ ID NO 43 (HCCI44)

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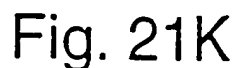
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GGGCCCATTGGGGAGTCCTGGCGGGCCTCGCCTACTATTCCATGGTGGGGAACTGGGC
TAAGGTTTTGTTGTGATGCTACTCTTTGCCGGCGTCGACGGGCATACCCGCGTGTGAG
GAGGGGCAGCAGCCTCCGATACCAGGGGCCTTGTTGCCCTCTTTAGCCCCGGGTGCGC
TCAGAAAATCCAGCTCGTAAACACCAACGGCAGTTGGCACATCAACAGGACTGCCCT
GAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGCCGCACTATTCTACAAACACAAA
TTCAACTCGTCTGGATGCCCAGAGCGCTTGGCCAGCTGTGCTCCATCGACAAGTTCC
CTCAGGGGTGGGGTCCCTCACTTACACTGAGCCTAACAGCTCGGACCAGAGGCCCTA
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CCGCCGCGAGGCAACTGGTTCGGCTGTACATGGATGAATGGCACTGGGTTACCAAGA
CGTGTGGGGGGCCCCCGTGCAACATCGGGGGGGCCGGCAACAACACCTTGACCTGCC



SECRET

ATGAGCACGAATCCTAAACCTCAAAGAAAAACCAAACGTAACACCAACCGCCGCCCA
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GCAGGGGCCCCAGGTTGGGTGTGCGCGCGACTAGGAAGACTTCCGAGCGGTGCGAAC
CTCGTGGGAGGCGACAACCTATCCCCAAGGCTCGCCGACCCGAGGGTAGGGCCTGGG
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GCTCCTGTACCCCCGCGGCTCTCGGCCTAGTTGGGGCCCTACAGACCCCCGGCGTAGG
TCGCGTAATTTGGGTAAGGTCATCGATACCCTTACATGCGGCTTCGCCGACCTCGTGG
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TGTATGAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTTCGGGA
GAACAACCTCTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCC
AGCGTCCCCACCACGACAATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTGCTT
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TTCACCATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATCTATC
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AACGGCCCTGGTGGTATCGCAGCTGCTCCGGATCCCACAAGCTGTCGTGGACATGGTG
GCGGGGGCCCCATTGGGGAGTCCTGGCGGGCCTCGCCTACTATTCCATGGTGGGGAACT
GGGCTAAGGTTTTGGTTGTGATGCTACTCTTTGCCGGCGTCGACGGGCATACCCGCGT
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Fig. 21L

TCGGCTCAGAAAATCCAGCTCGTAAACACCAACGGGCAGTTGGCACATCAACAGGACT
GCCCTGAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGCCGCACTATTCTACAAAC
ACAAATTCAACTCGTCTGGATGCCAGAGCGCTTGGCCAGCTGTGCTCCATCGACAA
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GCGGTCCAGTGTATTGCTTCACCCCGAGCCCTGTTGTGGTGGGGACGACCGATCGGTT
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ACGCGGGCCGCGCGAGGCAACTGGTTCGGCTGTACATGGATGAATGGCACTGGGTTCA
CCAAGACGTGTGGGGGGCCCCCGTGCAACATCGGGGGGGCCGGCAACAACACCTTGA
CCTGCCCCACTGACTGTTTTTCGGAAGCACCCCGAGGGCCACCTACGCCAGATGCGGTTT
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CCCTGCACTGTCAACTTCACCATCTTCAAGGTTAGGATGTACGTGGGGGGCGTGGAGC
ACAGGTTTCGAAGCCGCATGCAATTGGACTCGAGGAGAGCGTTGTGACTTGGAGGACA
GGGATAGATCAGAGCTTAGCCCGCTGCTGCTGTCTACAACAGAGTGGCAGATACTGCC
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TTATGGATGATGCTGCTGATAGCTCAAGCTGAGGCCGCTTAGAGAACCTGGTGGTCC
TCAATGCGGGCGGCGTGGCCGGGGCGCATGGCACTCTTTCCTTCTTGTGTTCTTCTGT
GCTGCCTGGTACATCAAGGGCAGGCTGGTCCCTGGTGCGGCATACGCCTTCTATGGCG
TGTGGCCGCTGCTCCTGCTTCTGCTGGCCTTACCACCACGAGCTTATGCCTAGTAA

Fig. 21L

Fig. 22

OD measured at 450 nm
construct

Fraction	volume dilution	39 Type 1b	40 Type 1b	62 Type 3a	63 Type 5a
START	23 ml 1/20	2.517	1.954	1.426	1.142
FLOW THROUGH	23 ml 1/20	0.087	0.085	0.176	0.120
1	0.4 ml 1/200	0.102	0.051	0.048	0.050
2		0.396	0.550	0.090	0.067
3		2.627	2.603	2.481	2.372
4		3	2.967	3	2.694
5		3	2.810	2.640	2.154
6		2.694	2.499	1.359	1.561
7		2.408	2.481	0.347	1.390
8		2.176	1.970	1.624	0.865
9		1.461	1.422	0.387	0.604
10		1.236	0.926	0.543	0.519
11		0.981	0.781	0.294	0.294
12		0.812	0.650	0.249	0.199
13		0.373	0.432	0.239	0.209
14		0.653	0.371	0.145	0.184
15		0.441	0.348	0.151	0.151
16		0.321	0.374	0.098	0.106
17		0.525	0.186	0.099	0.108
18		0.351	0.171	0.083	0.090
19		0.192	0.164	0.084	0.087

05899303-121204

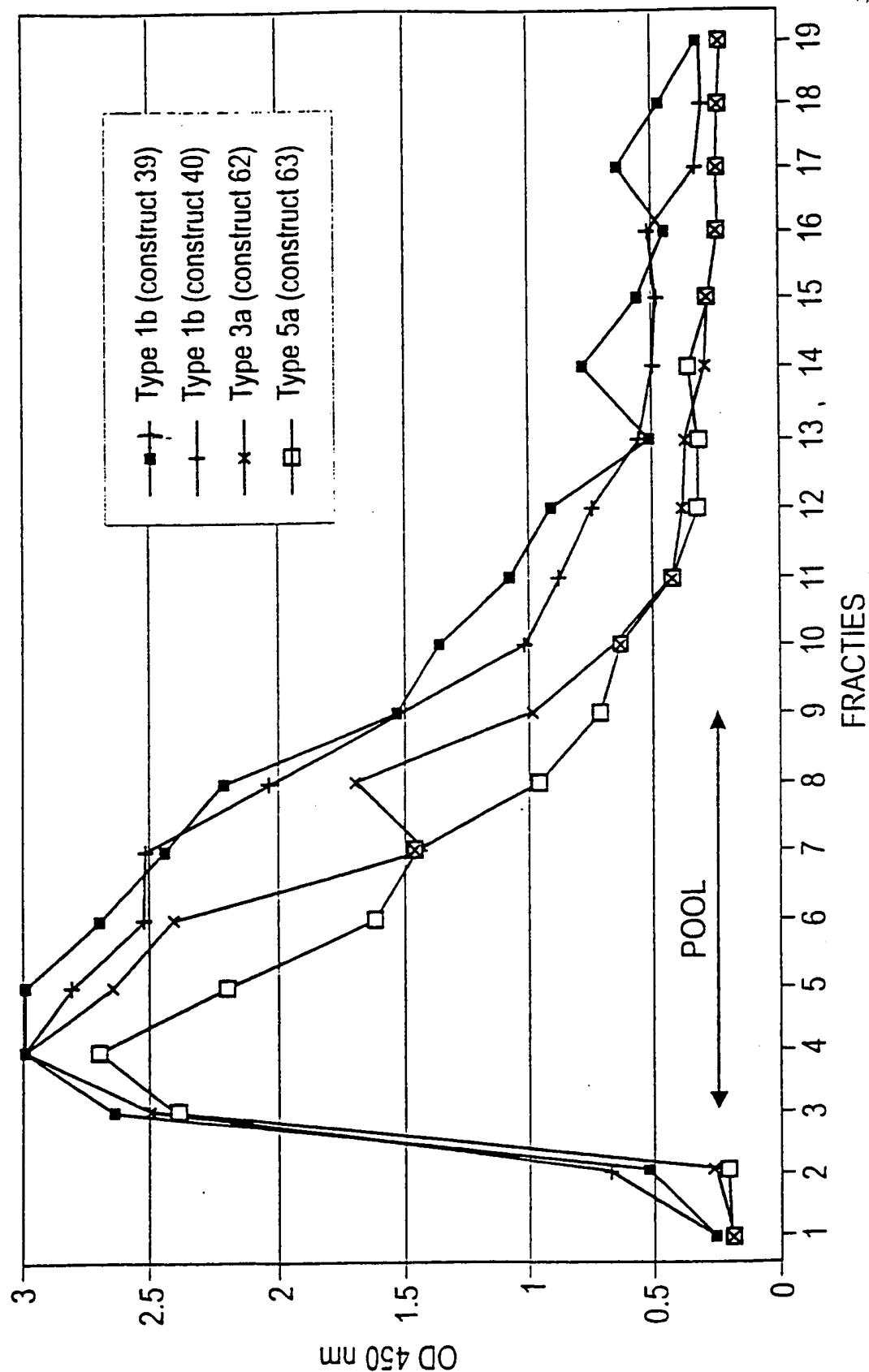


Fig. 23



Figure 24

Fraction	volume	dilution	OD measured at 450 nm			
			construct			
			39 Type 1b	40 Type 1b	62 Type 3a	63 Type 5a
20	250 μ l	1/200	0.072	0.130	0.096	0.051
21			0.109	0.293	0.084	0.052
22			0.279	0.249	0.172	0.052
23			0.093	0.151	0.297	0.054
24			0.080	0.256	0.438	0.056
25			0.251	0.100	0.457	0.048
26			3	1.649	0.722	0.066
27			3	3	2.526	0.669
28			3	3	3	2.345
29			3	3	2.849	2.580
30			2.227	1.921	1.424	1.333
31			0.263	0.415	0.356	0.162
32			0.071	0.172	0.154	0.064
33			0.103	0.054	0.096	0.057
34			0.045	0.045	0.044	0.051
35			0.043	0.047	0.045	0.046
36			0.045	0.045	0.049	0.040
37			0.045	0.047	0.046	0.048
38			0.046	0.048	0.047	0.057
39			0.045	0.048	0.050	0.057
40			0.046	0.049	0.048	0.049

102121 1026660

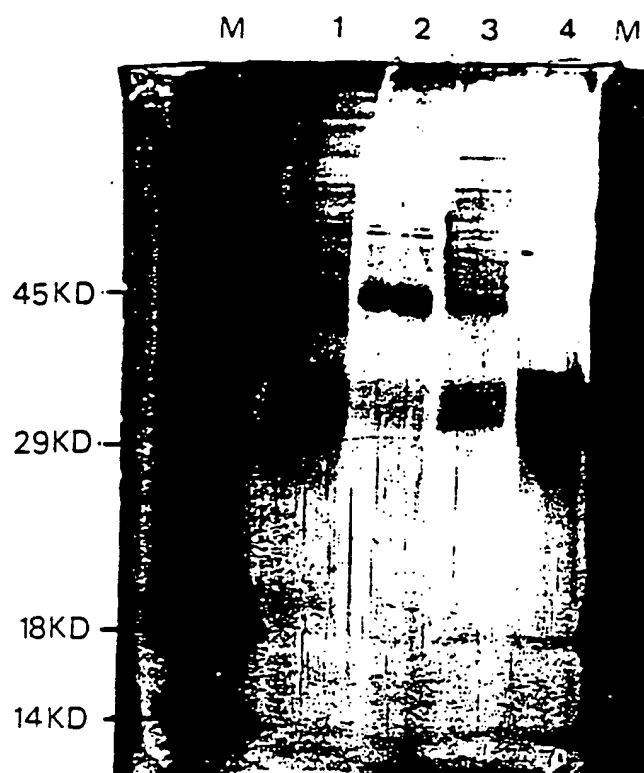


Fig. 26

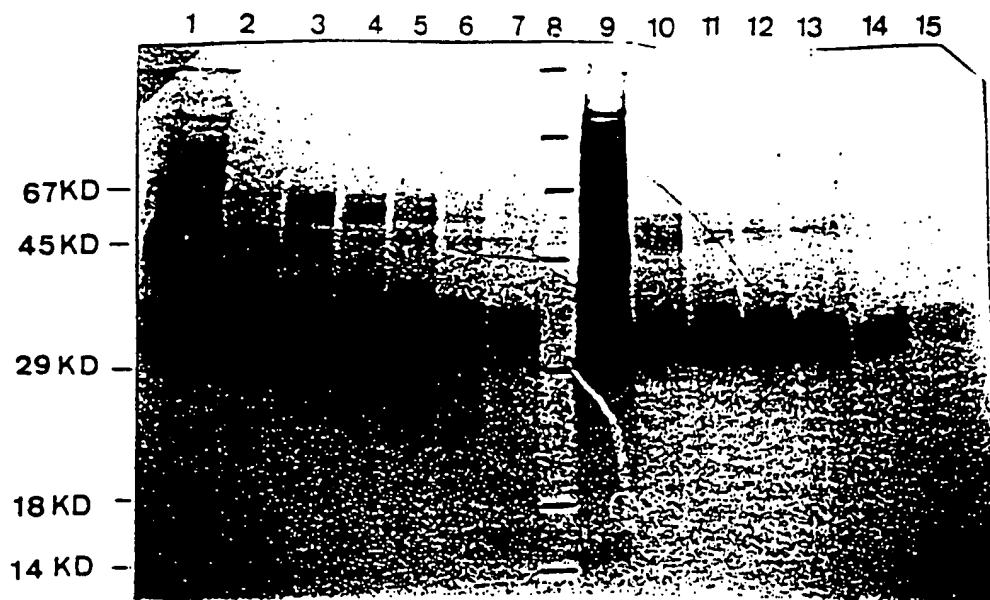


Fig.27

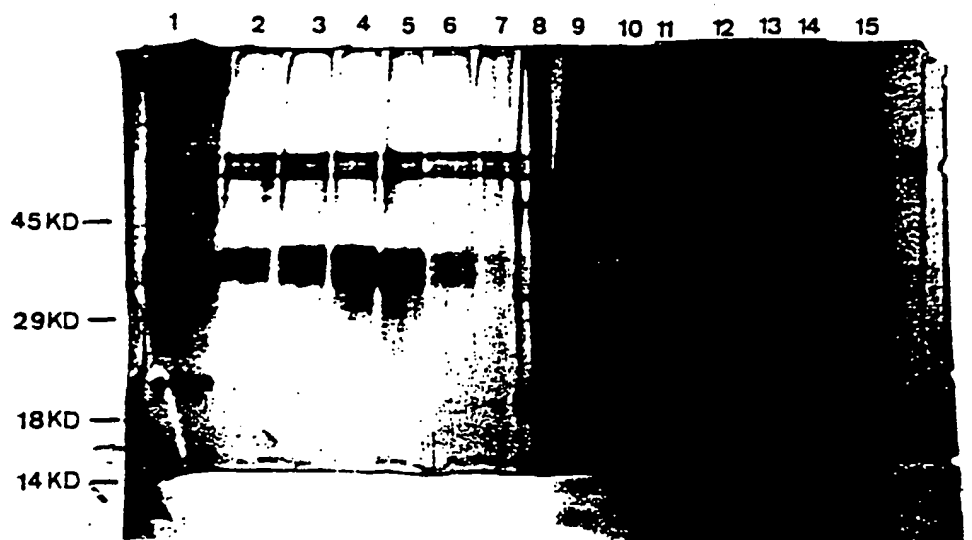


Fig.28

M 1 2 3 4 5 6

67 kD -

45 kD -

29 kD -

18 kD -

14 kD -

Fig.29

Lane 1: Crude Lysate
Lane 2: Flow through Lentil Chromatography
Lane 3: Wash with EMPIGEN Lentil Chromatography
Lane 4: Eluate Lentil Chromatography
Lane 5: Flow through during concentration lentil eluate
Lane 6: Pool of E1 after Size Exclusion Chromatography

09899303 121204

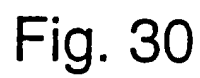


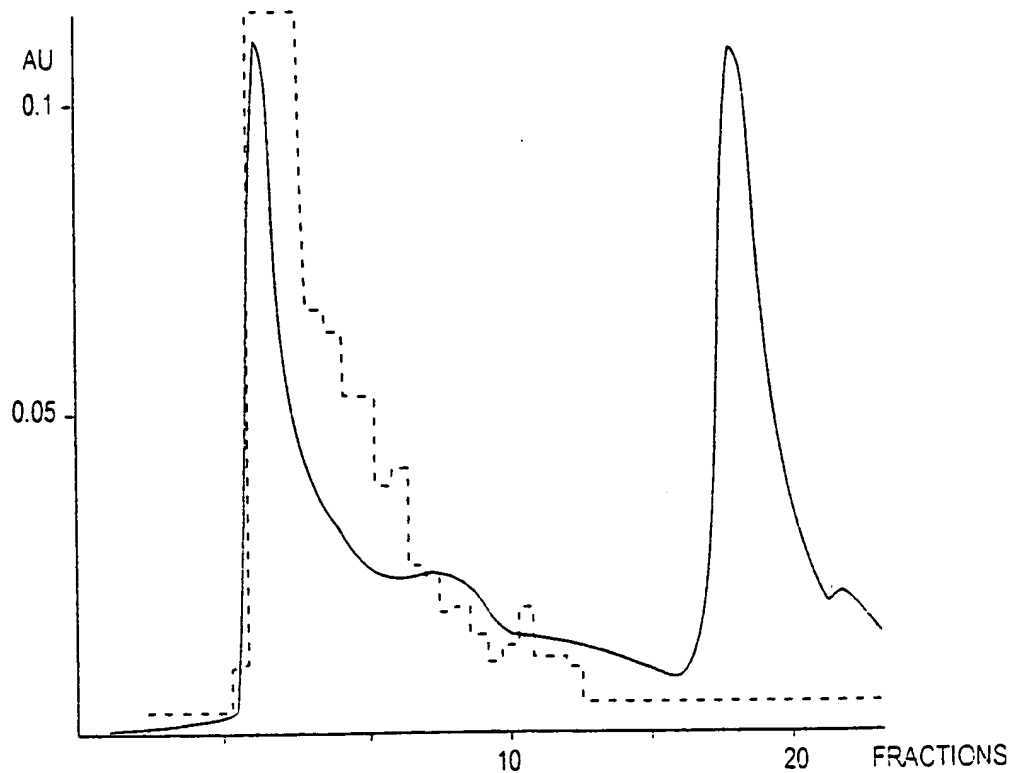
Fig. 30



NON - REDUCED

Fig. 31A

E2 + CONTAMINANTS (AGGREGATES)



REDUCED

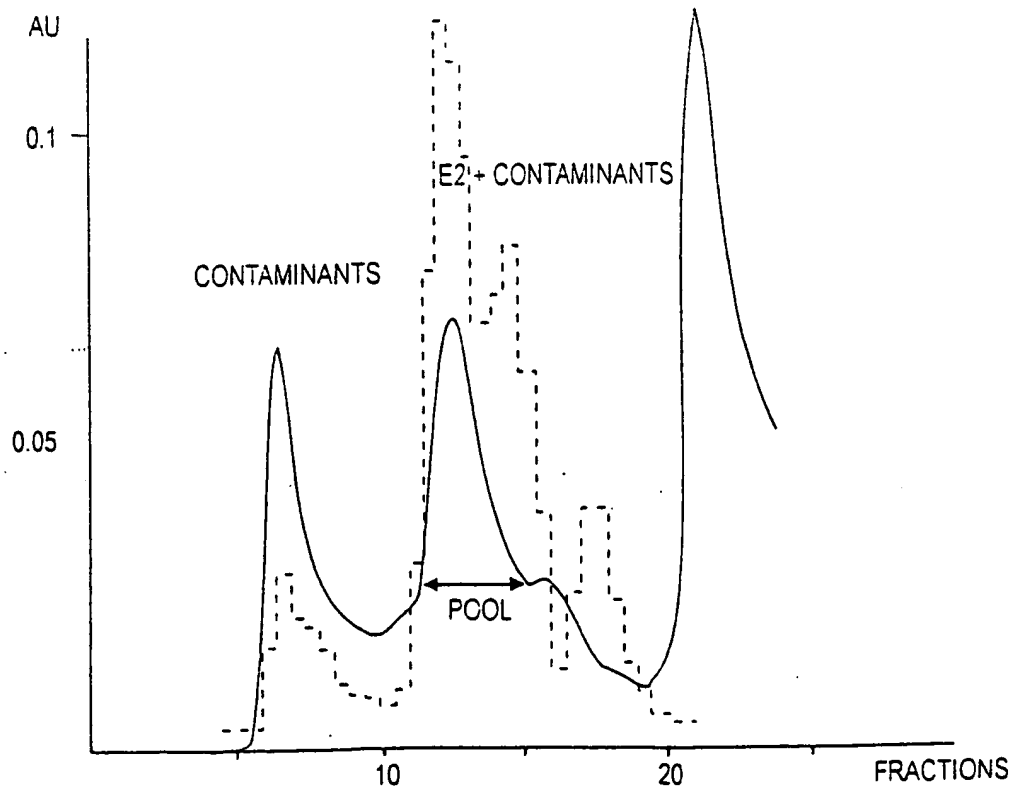


Fig. 31B

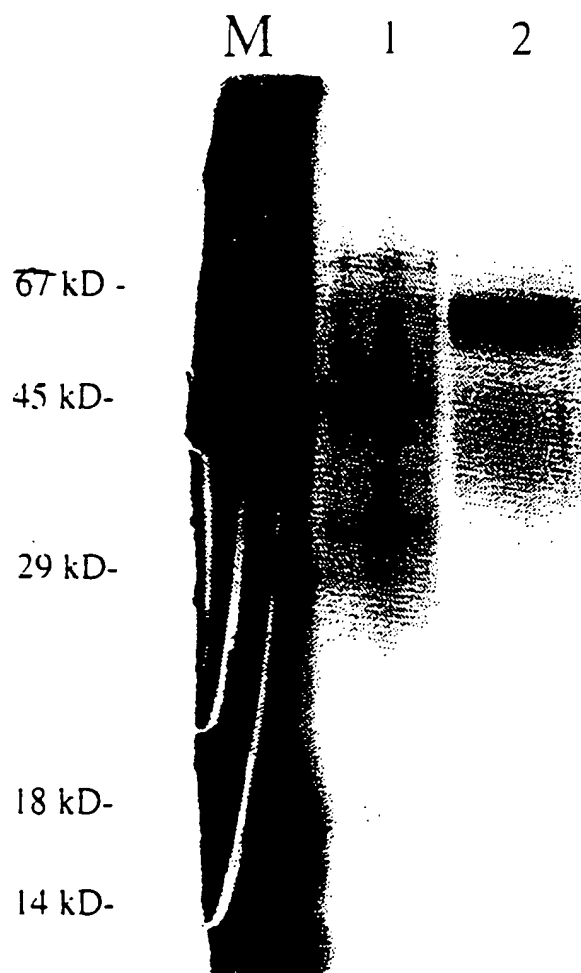
10241204 00000000

ME (m)

Fig. 32



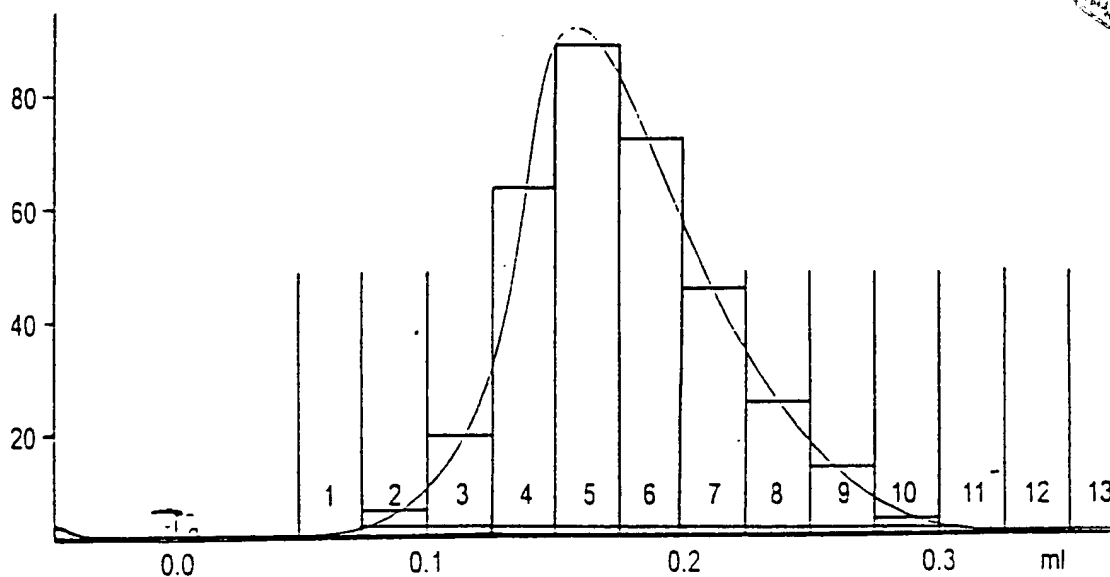
SILVER STAIN OF PURIFIED E2



1. 30 mM IMIDAZOLE WASH Ni-IMAC
2. 0.5 ug E2

Fig.33

09899303 124201



No.	Ret. (ml)	Peak start (ml)	Peak end (ml)	Dur (ml)	Area (ml* μ AU)	Height (μ AU)
1	-0.45	-0.46	-0.43	0.04	0.0976	4.579
2	1.55	0.75	3.26	2.51	796.4167	889.377
3	3.27	3.26	3.31	0.05	0.0067	0.224
4	3.33	3.32	3.33	0.02	0.0002	0.018

Total number of detected peaks = 4
 Total Area above baseline = 0.796522 ml* μ AU
 Total area in evaluated peaks = 0.796521 ml* μ AU
 Ratio peak area / total area = 0.999999
 Total peak duration = 2.613583 ml

Fig. 34

102441 056860

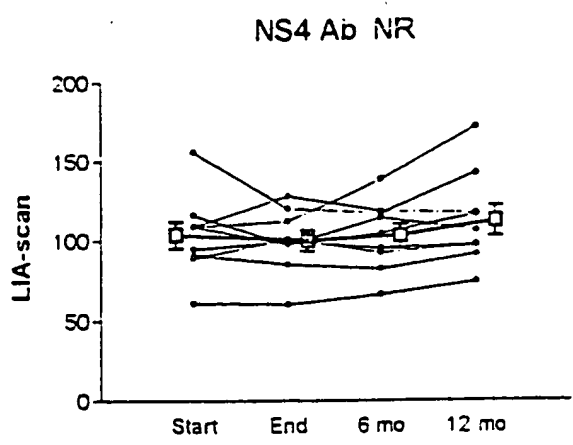


Fig. 35A-1

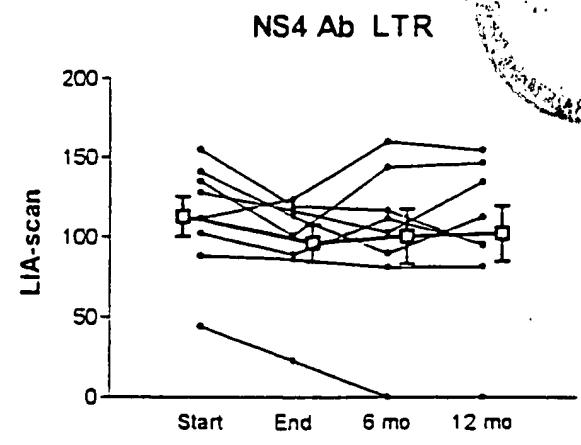


Fig. 35A-2

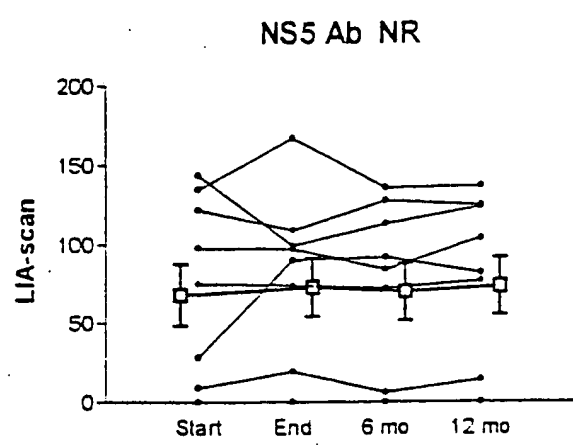


Fig. 35A-3

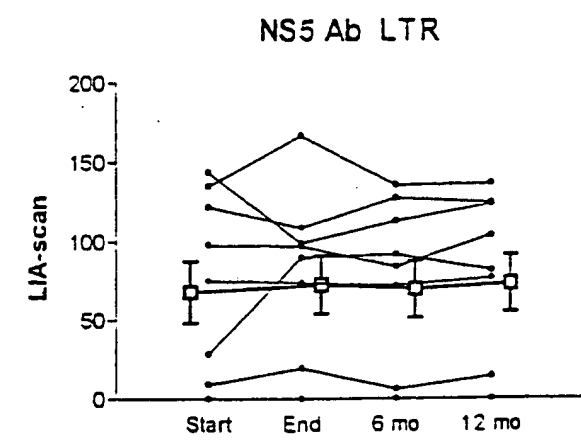


Fig. 35A-4

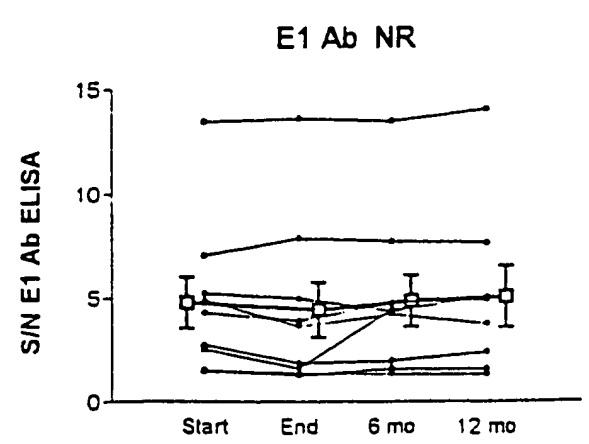


Fig. 35A-5

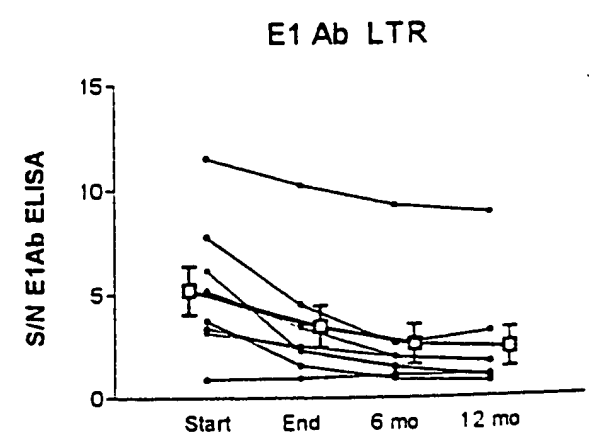


Fig. 35A-6

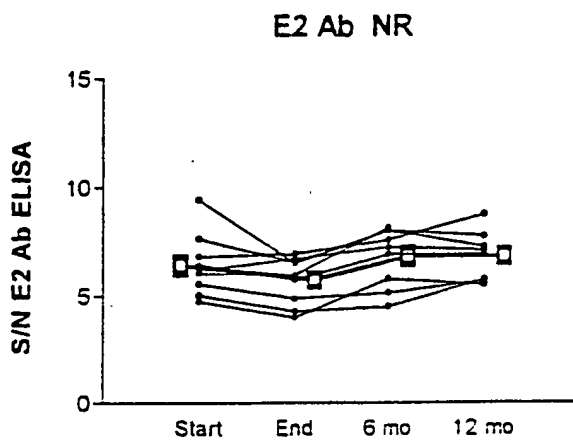


Fig. 35A-7

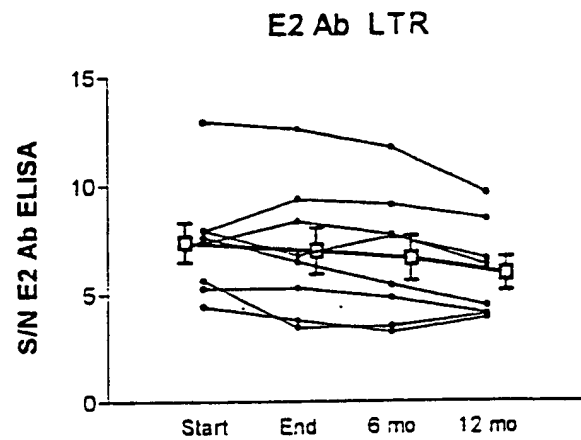


Fig. 35A-8

For file 005550

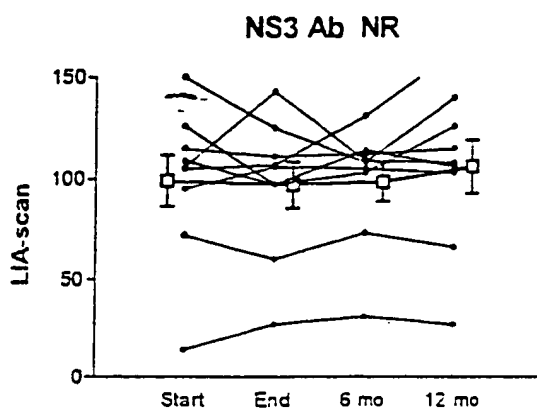


Fig. 35B-7

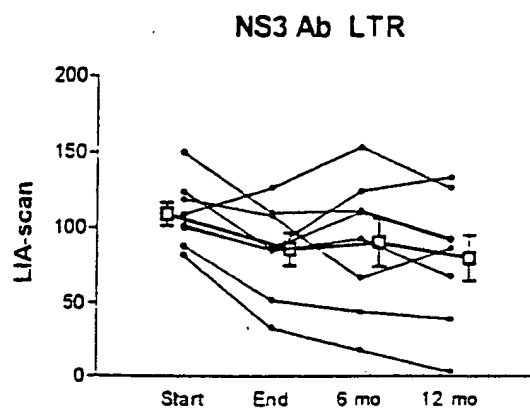


Fig. 35B-8

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Fig. 36A

E1 Ab

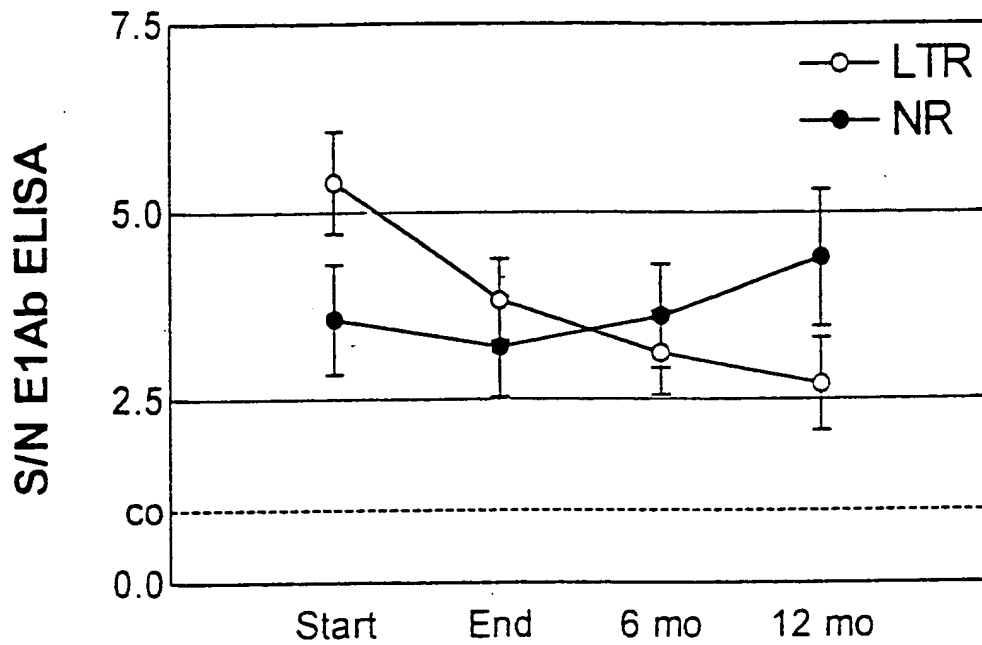


Fig. 36B

E2 Ab

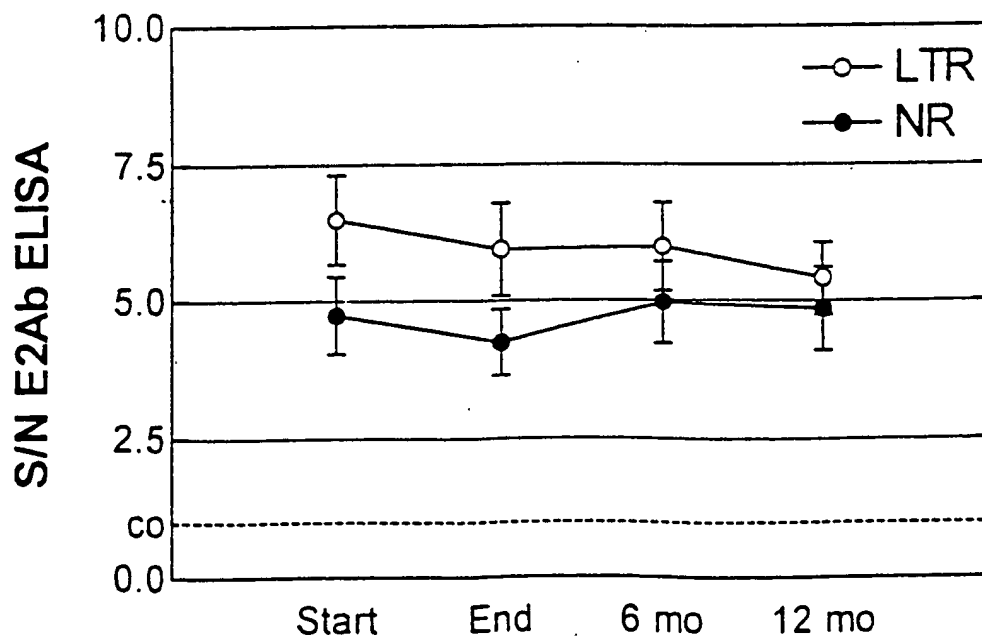


Fig. 37A

Non Responders

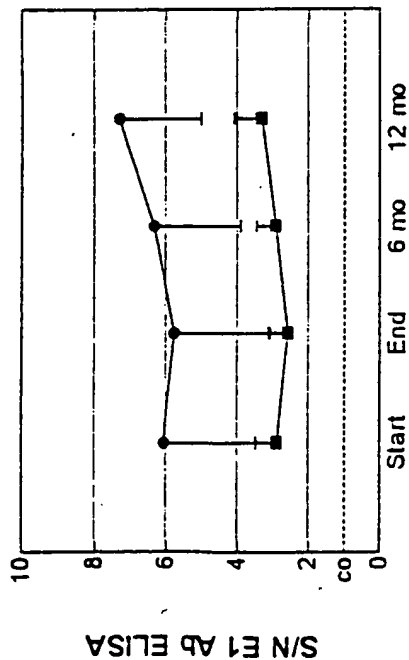


Fig. 37B

Long Term Responders

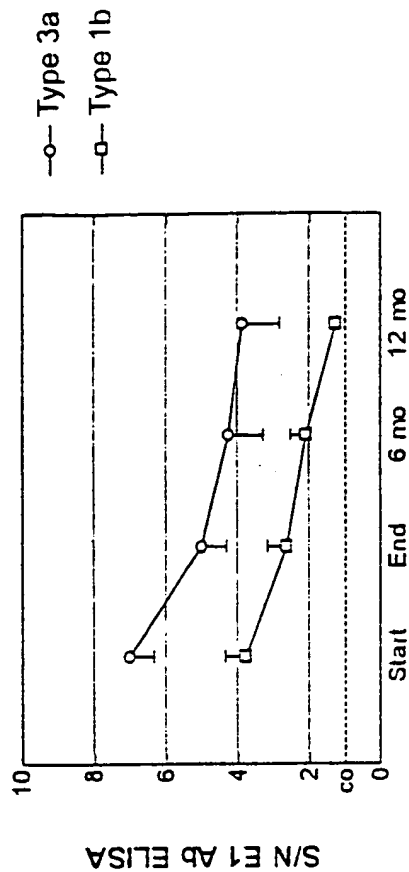


Fig. 37C

Type 1b

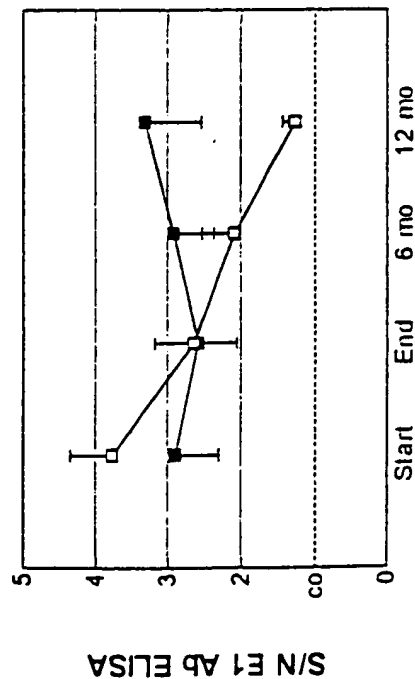
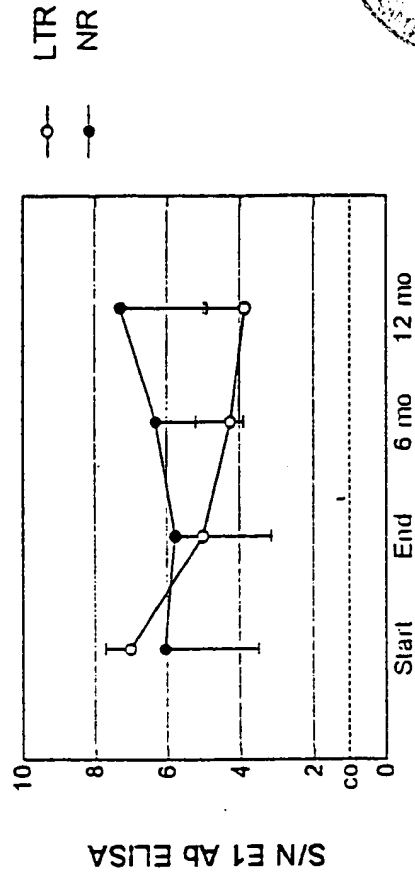
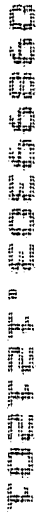


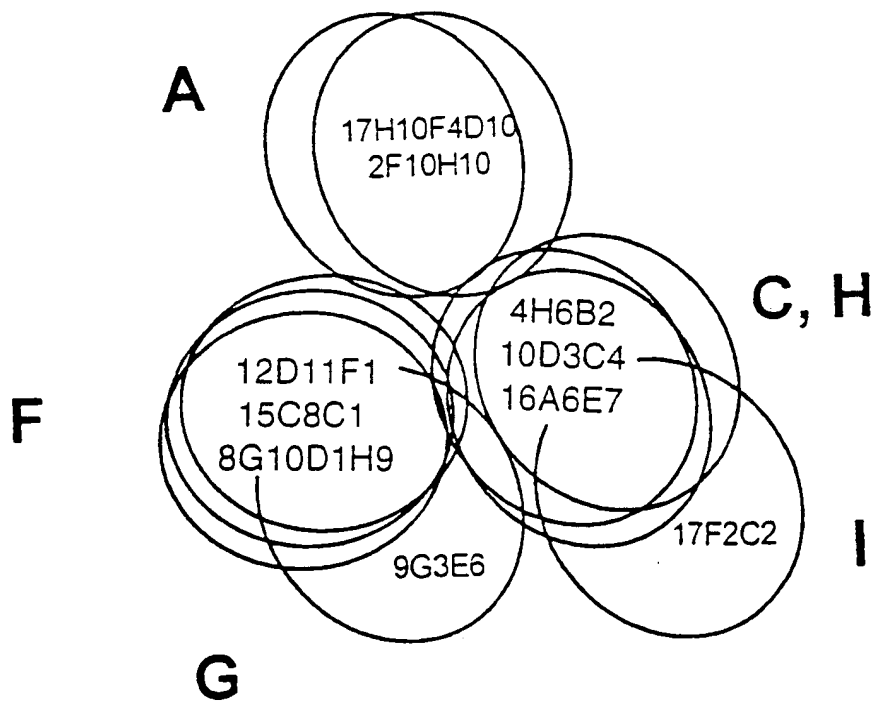
Fig. 37D

Type 3a



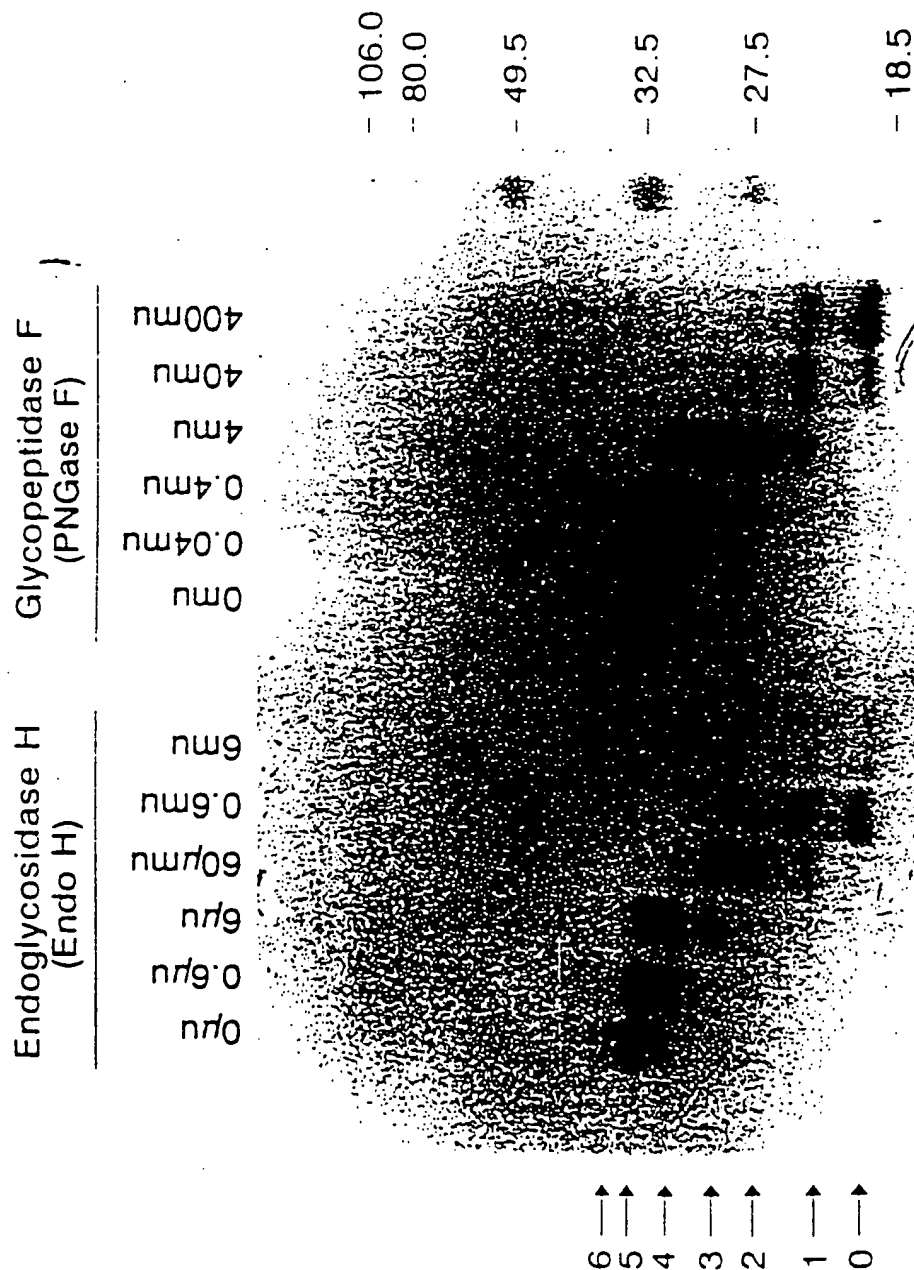


Relative Map Positions of anti-E2 monoclonal antibodies



PARTIAL DEGLYCOSYLATION OF HCV E1 ENVELOPE PROTEIN

Fig.39



PARTIAL TREATMENT OF HCV E2/E2s ENVELOPE PROTEINS BY PNGase F

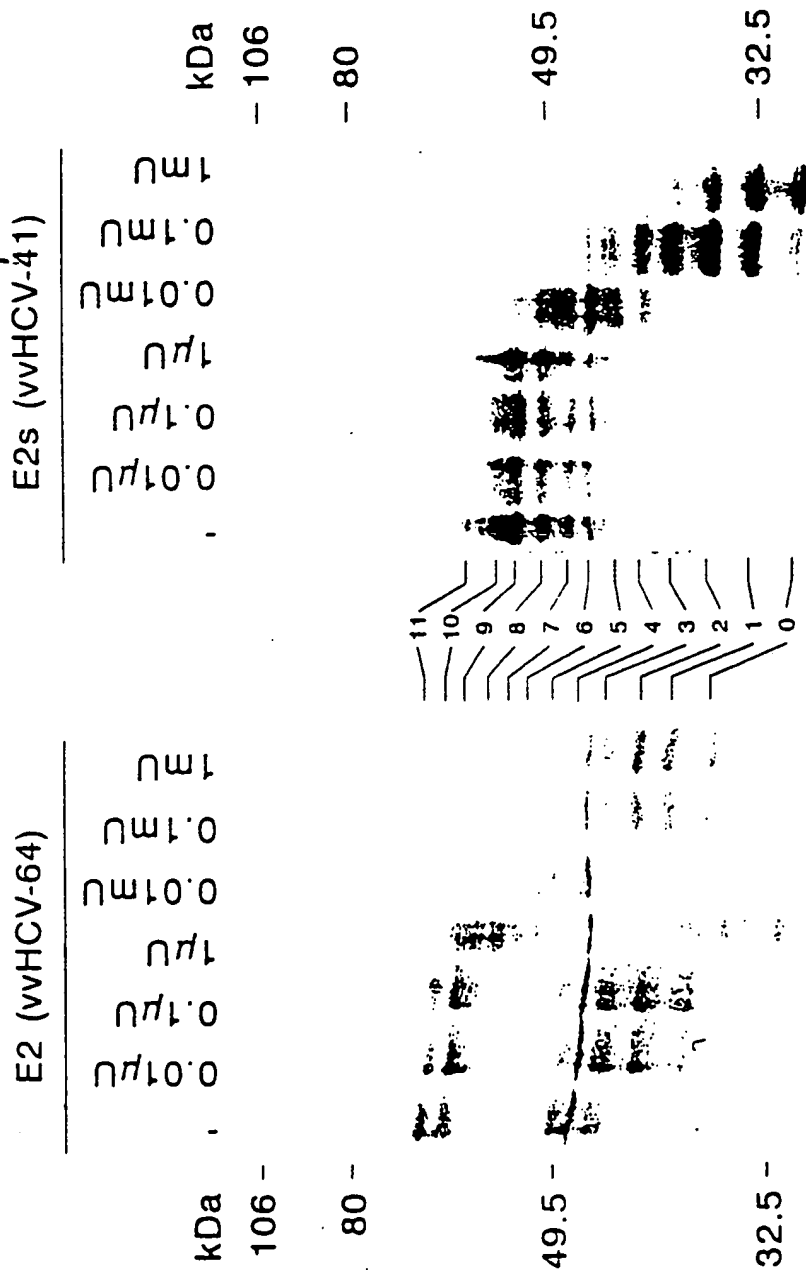


Fig. 40



Fig. 41 *In Vitro* Mutagenesis of HCV E1 glycoprotein

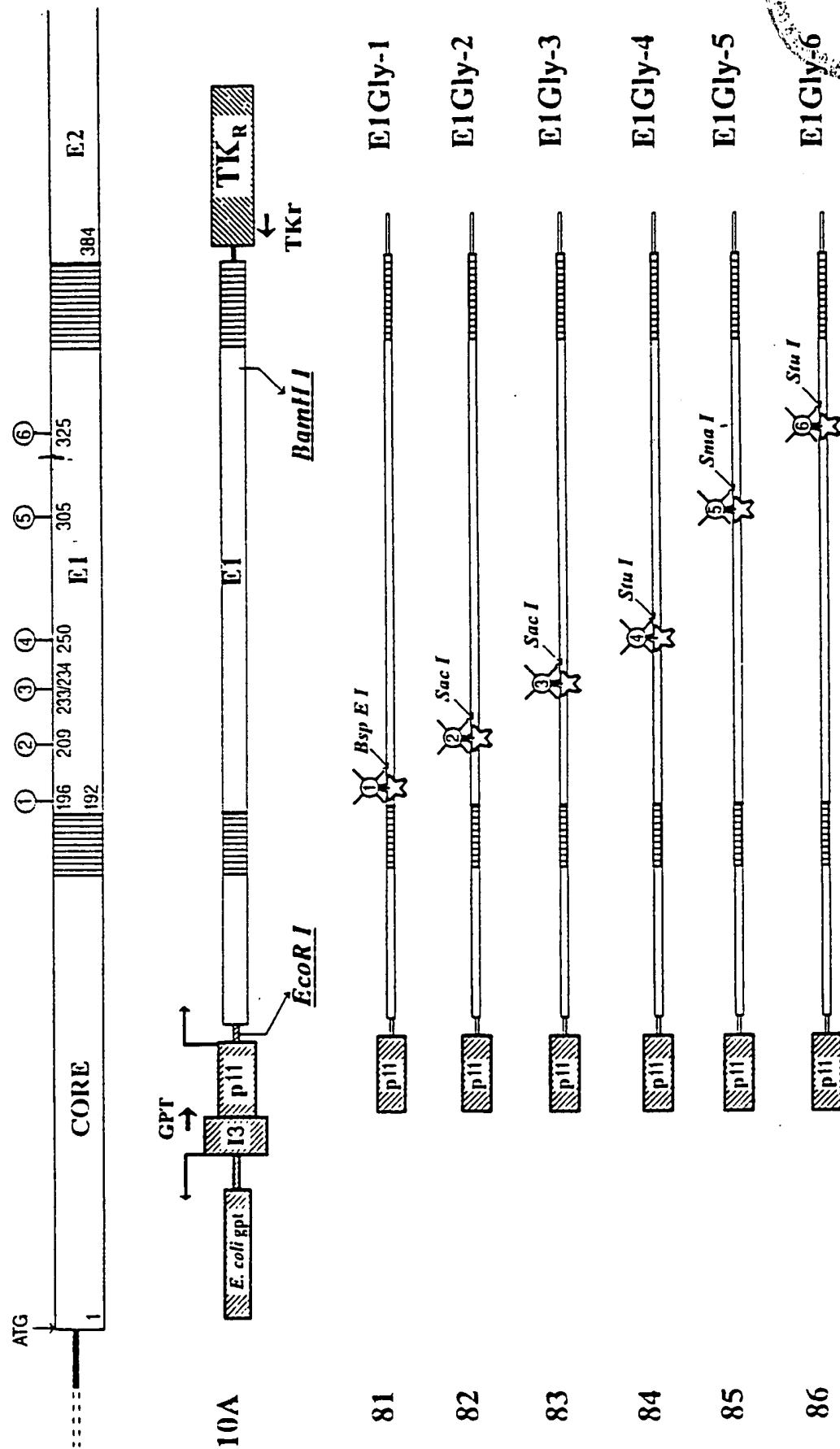
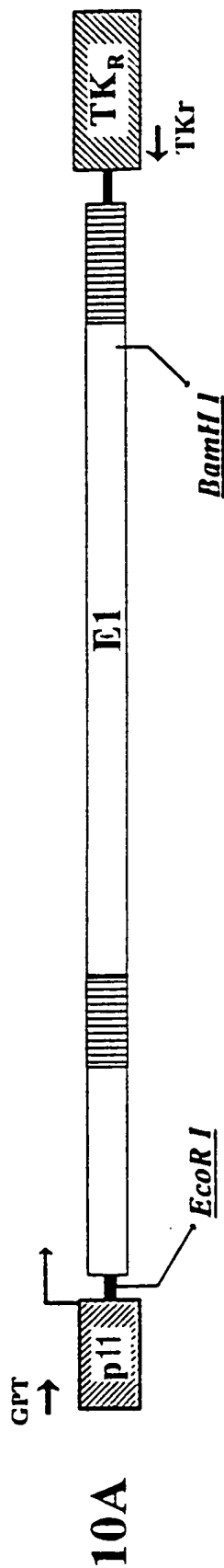
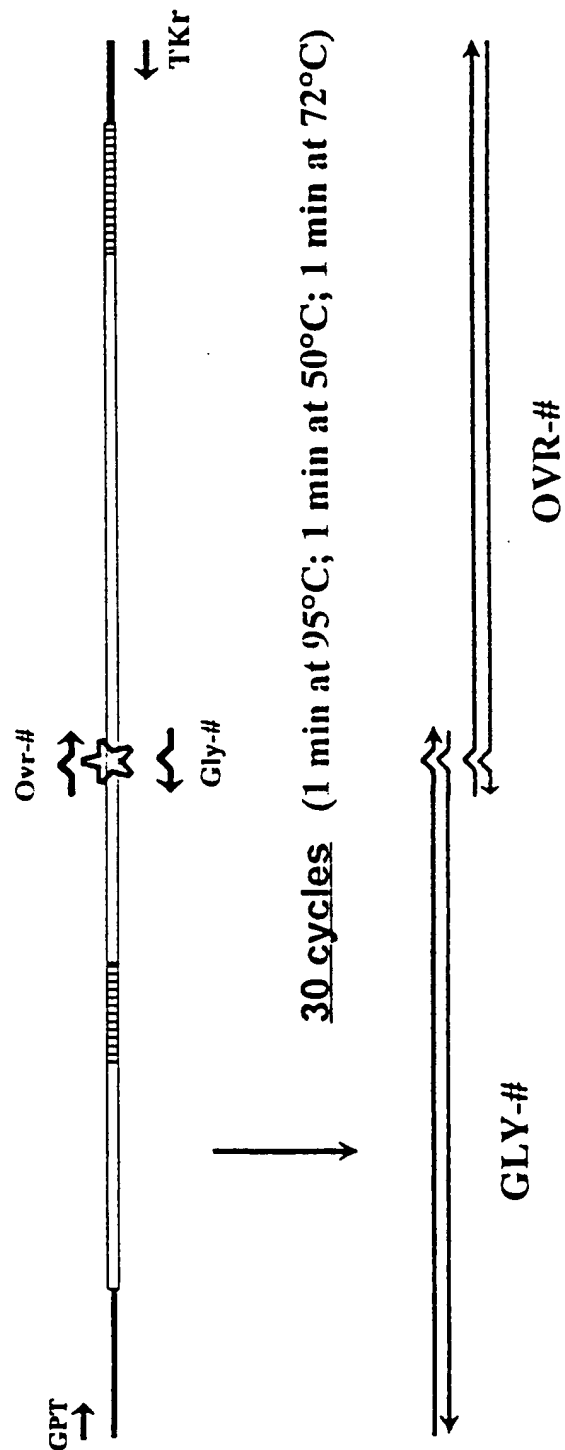


Fig. 42A *In Vitro* Mutagenesis of HCV E1 glycoprotein

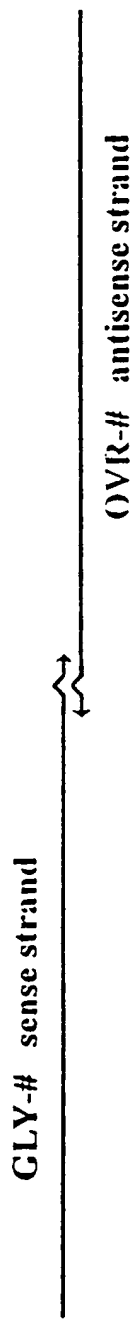


1. First step of PCR amplification (Gly-# and Ovr-# primers)



2. Overlap extension and nested PCR

a. Overlap extension Fig. 42B



↓
2 cycles (1 min at 95°C; 1 min at 50°C; 1 min at 72°C)



b. Nested PCR amplification (GPT-2 and TKR-2 primers)

↓
25 cycles (1 min at 95°C; 1 min at 55°C; 1 min at 72°C)

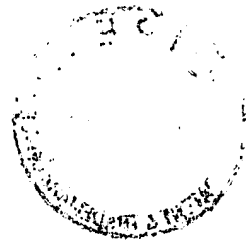
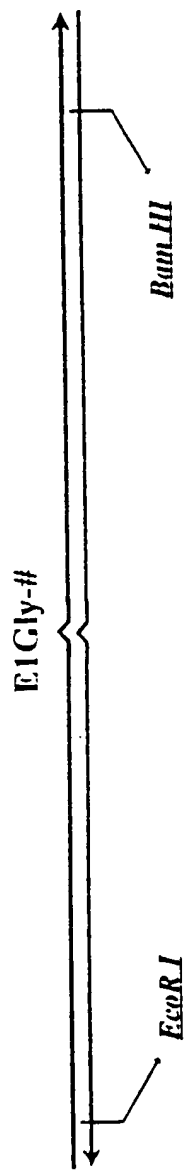
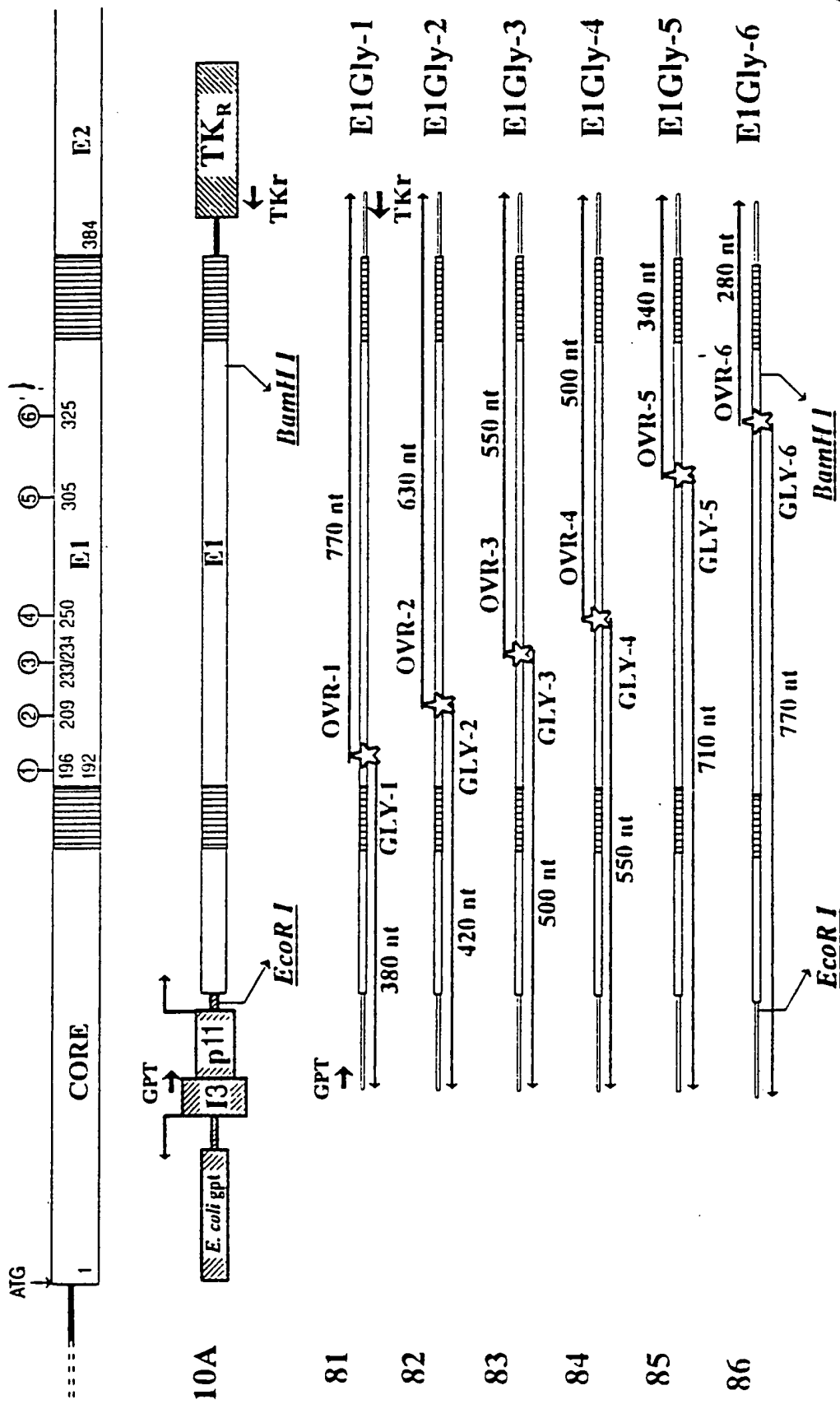


Fig. 43 *In Vitro* Mutagenesis of HCV E1 glycoprotein



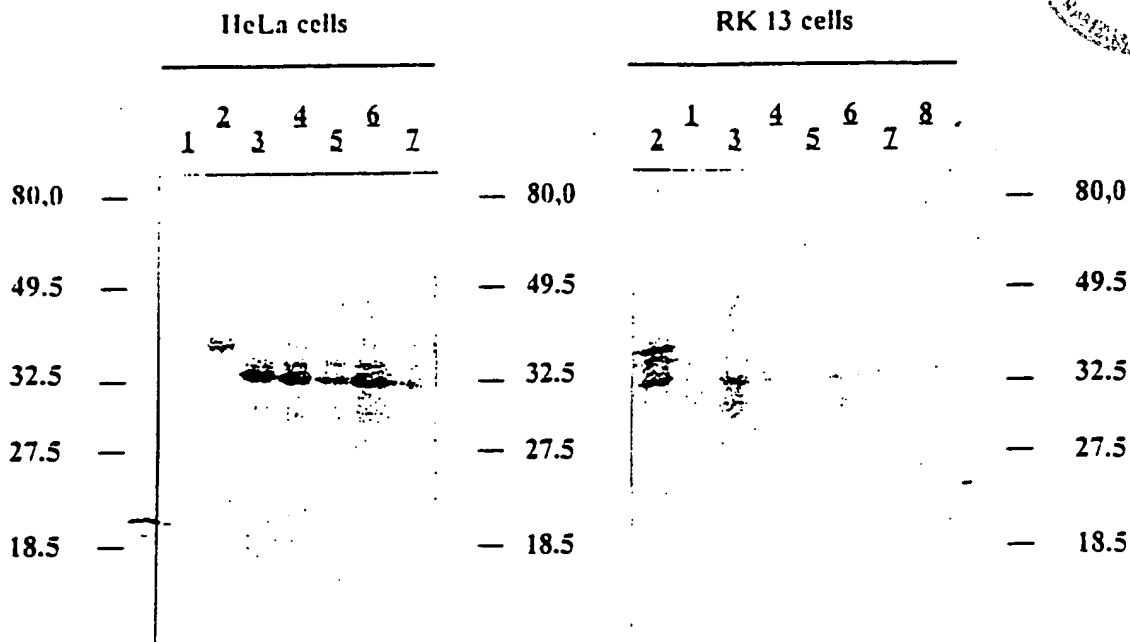


Fig.44A

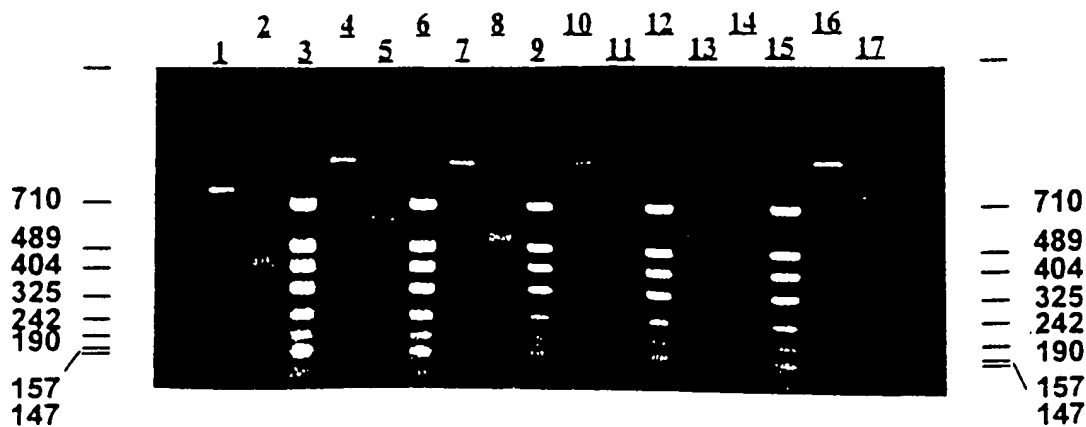


Fig.44B

Fig. 45

Fig. 46